# STUDIES ON THE PERIPHERAL CIRCULATION DURING PREGNANCY

by

Christine Averil Snodgrass, M.B., Ch.B. (Edinburgh)

from

The Institute of Obstetrics and Gynaecology,
University of London, Hammersmith Hospital, London.

A thesis presented for the degree of Doctor of Medicine
in the Faculty of Medicine, University of Edinburgh, 1968.

I certify that this thesis entitled "Studies on the Peripheral Circulation During Pregnancy" was composed by

Christine Averil Snodgrass, M.B., Ch.B., M.R.C.O.G.,

from the results of her own research work in this Department.

CONTENTS

Contents, cont.

# GLOSSARY

## Accepted statistical abbreviations

b = regression coefficient

F = variance ratio

S.D. = standard deviation

S.E. = standard error of the mean

t = Student's t

P = probability

## Electronic abbreviations

A = ampere

D.C. = direct current

E = earth

F = farad

F.S.D. = full scale deflection

H.S. = high stability

K = kilo ohm

L = line

mV = millivolts

N = neutral

r.p.m. = revolutions per minute

SKTS = sockets

V = volts

W = watts

Y.S.I. = Yellow Springs Instruments

ZD = Zenerdiode

Ω = ohm

F = microfarad

## Others

°C. = degrees Centigrade

cu.mm. = cubic millimetre

°F. = degrees Fahrenheit

g. = gramme

kg. = killogramme

lb. = pound

mg. = milligramme

min. = minute

ml. = millilitre

mm. = millimetre

mm.Hg. = millimetres of mercury

m = millimicron

µg. = microgramme

µµg. = micro-microgramme

N = normal solution

n = number

# INTRODUCTION

## INTRODUCTION

When this study began there were only three published reports on peripheral blood flow in pregnancy and the results were conflicting. Only Burt (1950) had specifically examined patients with hypertension and reported the interesting finding that fore-arm flow rates were increased in the isolated recordings she had made. It was thought profitable to pursue this finding further and to elucidate behaviour in normal pregnancy, also by an experiment designed to measure flow rates in the same subjects at frequent intervals during pregnancy. As there was no information in the literature regarding the possible effect of other pregnancy changes on the peripheral circulation, it was decided to investigate haematological changes, including total blood volume, body temperature changes, pregnanediol excretion and cytological hormone assessments concurrently with the peripheral circulation study. Since the study began three further reports have appeared in the literature, again with conflicting results. None of these workers have used an entirely acceptable experimental design and none has attempted concurrent investigations into other factors which might influence the results.

The water-bath plethysmograph has been used in this study as reproducible results are obtainable over long periods of time and the accuracy of the method has been validated by experiment described in the text.

One hundred and twenty-eight subjects have been examined on over 1,340 occasions. This entailed the recording and calculation of over 30,000 flow curves apart from the measurements of other parameters.

In the statistical analysis trends within groups have been analysed by within patient change by means of the paired t-test. Between group analysis has been carried out by means of unpaired t-tests. Analysis of variance has been used to elucidate problems only when each subject is represented by a simple statistic; that is, when the degrees of freedom are related to the number of subjects and not made artificially large by multiple readings from the same subject. Regression analysis has been used to confirm or refute correlations between two parameters. For the analysis of grwoth curves use has been made of the method described by Hills (1968). Statistical tables used have been those of Fisher and Yates and Documenta Geigy.

# DEFINITION OF BLOOD PRESSURE GROUPS

## DEFINITION OF BLOOD PRESSURE GROUPS

### Normotensive Group

Patients in whom the blood pressure was not recorded above 120/80 mm. Hg, on more than one occasion in the ante-natal period.

### Hypertension I Group

Patients in whom the blood pressure was recorded above 120/80 mm. Hg. on two occasions or more during the ante-natal period and at least once before 20 weeks gestation. The group includes patients in whom either the systolic or diastolic pressure alone was above 120/80 mm. Hg. if neither pressure was below this level. For example, blood pressures of 130/80 mm. Hg. were classified as hypertensive but blood pressures of 140/75 mm. Hg. were excluded.

### Hypertension II Group

Patients in whom the blood pressure was recorded above 120/80 mm. Hg. on two or more occasions after 20 weeks gestation only.

### Control Group

A group of healthy, non-pregnant women of the same age range as the pregnant group. Subjects in whom a blood pressure was recorded as over 120/80 mm. Hg on two or more occasions were considered hypertensive and were equivalent to the Hypertension I group of the pregnant subjects.

SUMMARY

## SUMMARY


### Experimental Design

The resting fore-arm blood flow rates were measured at four weekly intervals throughout pregnancy and at increasing intervals up to 40 weeks after delivery. Twenty-six subjects were normotensive as defined on page 5 , twenty-four subjects were included in the hypertension I group and thirty-six subjects were included in the hypertension II group. Control groups of twenty-two normotensive and ten hypertensive non-pregnant subjects were also studied.

The resting hand blood flow rates were measured in the same intervals during and after pregnancy in three normotensive subjects, six subjects in the Hypertension I group and nine subjects in the Hypertension II group. The non-pregnant control group consisted of nine subjects who were normotensive and six subjects who were hypertensive.

At the same time, measurements were made of blood volume by means of Evans Blue Dye and the haemoglobin, red cell count and packed cell volume estimated. Assessment of hormonal function was made in all subjects by measurement of the cornification index and in 34 subjects by pregnanediol excretion.

### Results

#### I - Fore-Arm Blood Flow Rates

(a) Control Group

The non-pregnant resting fore-arm blood flow rate was 3.9 mls. per 100 mls./minute in the normotensive group and 4.0 mls./100 mls. per minute in the hypertensive group. There was a small but

significant reduction in fore-arm blood flow rate with increasing age but, over a six month period fore-arm flow rates were reproducible within subjects. Fore-arm skin temperature rose with increasing fore-arm blood flow and decreasing difference between oral and fore-arm skin temperature. No significant relationship could be demonstrated between fore-arm blood flow rates and parity, body surface area, smoking habits, stage of menstrual cycle, season, normal body temperature, pulse rate, pulse pressure, blood pressure, blood volume or haemoglobin level.

(b) Pregnant Groups

The mean fore-arm blood flow rates in early pregnancy did not differ between the blood pressure groups but all were significantly lower than the non-pregnant mean flow rate and that for 40 weeks after delivery. There was a significant increase in the mean fore-arm blood flow rate with advancing pregnancy in all blood pressure groups, the maximum levels being attained near term. The amount of change from the first visit to 32 - 35 weeks gestation did not differ between blood pressure groups but thereafter the mean flow rates were significantly different. The maximum level attained by the normotensive group never exceeded the non-pregnant mean. The maximum level attained by the hypertension I group was above the non-pregnant mean but not significantly so. The mean flow rate for the hypertension II group rose significantly above the non-pregnant and normotensive pregnant mean flow rates. On the third post-natal day, the hypertensive groups showed a decrease in mean flow rate and all groups had attained non-pregnant control group levels at 40 weeks after delivery.

The differences in changes in the fore-arm blood flow rates in the three blood pressure groups could not be ascribed to differences in age, parity, height, weight, surface area, season, stress, smoking habits, haemoglobin levels or blood volume change.

The fore-arm blood flow rates during pregnancy increased with increasing diastolic pressure, with decreasing change in pregnanediol levels and decreasing change in cornification index.

There was no relationship between the change of fore-arm blood flow and systolic pressure change, pulse rate change, blood volume change, change in oral temperature, weight gain or birth weight. No relationship could be demonstrated between fore-arm blood flow rates and breast feeding, artificial feeding or resumption of the menstrual cycle.

Compared with normotensive pregnancy significantly higher fore-arm flow rates were found in four subjects who aborted, one subject who had an accidental ante-partum haemorrhage, one subject who had a twin pregnancy, one subject who had a stillbirth due to placental insufficiency and one subject with latent diabetes. One subject who was examined before abortion of a molar pregnancy had a flow rate within normotensive range for that gestation.

## II - Hand Blood Flow Rates

### (a) Control Groups

The mean hand flow rates in the normotensive and hypertensive control group were not significantly different; the mean for the whole non-pregnant group was 9.2 mls./100 mls./minute. There was a significant decrease in hand flow rate in the post-ovulatory phase

of the menstrual cycle but no significant relationship could be demonstrated between non-pregnant hand blood flow rates and age, parity, body surface area, smoking habits, normal body temperature, pulse rate, pulse pressure or blood pressure.

(b) Pregnant Groups

The numbers of subjects examined in each blood pressure group were small and as no gross differences were apparent between the groups the results were considered together. In early pregnancy there is no significant change from the mean non-pregnant flow rate but after 19 weeks gestation the mean flow rate rose sharply, reaching a maximum at 36 - 39 weeks gestation. On the third day after delivery there was little change in mean hand flow rate but non-pregnant levels were attained by 6 weeks after delivery. No relationship could be demonstrated between change in hand flow rates and change in blood pressure, pulse rate, body weight, body temperature; nor with parity or smoking habits or birth weight.

III - Blood Pressure

(a) In the blood pressures recorded at the time of flow measurement, no significant change occurred throughout pregnancy in the normotensive group nor the hypertension I group. A significant change occurred in systolic and diastolic pressures of the hypertension II group. The change in systolic level preceded the change in diastolic level by 8 weeks.

(b) When all blood pressures recorded during pregnancy were taken into account, significant rises occurred in all three blood pressure groups. The diastolic rose the most, giving a relative decrease in pulse pressure with advancing pregnancy. Again, the

rise in systolic pressure preceded the rise in diastolic pressure by 8 weeks and significant elevations occurred before the subjects showed levels considered clinically hypertensive.

IV - Fore-Arm Peripheral Resistance

Fore-arm peripheral resistance units in all groups were higher than non-pregnant levels early in pregnancy and fell during pregnancy but significant effects were found only in the normotensive group and only transiently in the Hypertension I group. On the whole, peripheral resistance units were highest in the normotensive group and lowest in the Hypertension II group. Forty weeks after delivery the peripheral resistance units were the same as the control group.

V - Pulse Rate

Pulse rate was already elevated above non-pregnant levels at 8 weeks gestation. There was a slight but insignificant rise during pregnancy. Only from 12 to 19 weeks gestation was there a significantly higher rate found in the hypertension groups compared with the normotensive. By three days after delivery there was a fall in pulse rate. At 40 weeks after delivery the normotensive group approximated the non-pregnant levels but both hypertensive groups remained significantly higher than the normotensive non-pregnant control group but not higher than the hypertensive non-pregnant group.

VI - Oral Temperature

The oral temperature in early pregnancy was significantly higher than the non-pregnant control level and a significant fall

occurred throughout pregnancy. No significant difference was present between the blood pressure groups.

VII - Fore-Arm Temperature

Fore-arm temperature was measured in a small number of patients only. No significant change occurred during pregnancy but the overall mean pregnancy fore-arm temperature was highest in the Hypertension II group and lowest in the Hypertension I group. The difference was significant.

VIII - Blood Volume

The blood volume at 8 - 11 weeks gestation was the same as that for 12 weeks after delivery. A small but significant increase occurred from 8 - 11 to 12 - 15 weeks gestation. Thereafter the blood volume rose more rapidly reaching a maximum at 28 - 31 weeks gestation, after which there were slight but insignificant changes as term approached. After delivery the blood volume fell rapidly, reaching non-pregnant levels at 6 weeks after delivery.

There was a significant relationship between blood volume and surface area in the non-pregnant state but no relationship was found between thechange in blood volume during pregnancy and surface area at the first visit or increase in body weight during pregnancy. No relationship was found between change in blood volume and parity, birth weight, change in fore-arm flow rate or change in pregnanediol level. The maximum increase in blood volume during pregnancy did not differ between the blood pressure groups.

IX - Haemoglobin

The haemoglobin level fell from 8 - 11 weeks gestation and

maintained its lowest levels from 20 - 31 weeks gestation, thereafter rising to first visit levels. After delivery the mean haemoglobin level rose to a maximum at 6 weeks and this level was maintained to 40 weeks after delivery. The drop in haemoglobin level occurred despite prophylactic oral iron given to all patients and did not reflect the changes in blood volume after 31 weeks gestation.

X - Red Cell Count and Packed Cell Volume

The red cell count behaved exactly as the haemoglobin level. The packed cell volume behaved similarly but there were significant differences between the blood pressure groups, the mean packed cell volume for the whole of pregnancy being highest in the Hypertension I group and lowest in the Hypertension II group.

XI - Mean Corpuscular Haemoglobin Concentration, Mean Corpuscular Haemoglobin and Mean Cell Volume

The mean corpuscular haemoglobin concentration did not change during or after pregnancy. The mean corpuscular haemoglobin rose during pregnancy but a similar change was demonstrated in the non-pregnant control group and conclusions are difficult to draw. The mean cell volume also rose during pregnancy but again there were similar significant changes in the non-pregnant group.

XII - White Cell Count

The white cell count was already raised at 8 - 11 weeks gestation compared with both the non-pregnant level and the post-natal means. There was another significant increase in white cell count during pregnancy reaching a maximum at 32 - 35 weeks gestation. A further significant rise occurred by the third day after delivery

but by six weeks post-natally the white cell count had fallen to non-pregnant control group levels. It is noteworthy that during pregnancy the highest mean obtained was 9.74 thousand/cu.mm. ± S.D. 2.14 and the 99% upper confidence limit was 10.41 thousand/cu.mm.

XIII - Weight Gain

Weight gain in pregnancy showed no difference between the blood pressure groups, neither were the mean weights for each group different. Weight gain was controlled by diet as far as possible.

XIV - Pregnanediol

Serial pregnanediol estimations showed significant increases in early pregnancy followed by a steep rise towards term when there was a decrease in the rate of increase. The difference in the amount of increase in the blood pressure groups was just not significantly different.

XV - Cornification Index

The cornification index was already considerably below non-pregnant levels by 8 - 11 weeks gestation and continued to fall during pregnancy.

# METHOD AND EXPERIMENTAL DESIGN

## METHOD

### Choice of Method

Venous occlusion plethysmography is the most reliable method of quantitatively estimating blood flow rates (Barcroft and Swan, 1953; Figar, 1959; Greenfield, 1960; and Shepherd, 1963). It allows comparisons to be made over long periods of time, is simple, and acceptable to the patient.

### Basic Principles

Occlusion of venous flow causes blood to collect in the veins distal to the obstruction. The rate of increase in volume of the organ is equivalent to the amount of arterial inflow. A recording can be obtained by water or air displacement. This shows a linear response until the veins are almost fully distended when there is a gradual decrease in flow until the back pressure in the veins equals the arterial inflow pressure and the recording becomes horizontal. Thus, arterial inflow rate to the organ is measured over the initial part of the curve.

### The Apparatus: General

The fore-arm is enclosed in a sleeve sealed to the surrounding water-bath and for hand flow measurements the sleeve is replaced by a glove. The apparatus is filled with water from which all air bubbles have been expelled and the only outlet from the water-bath which is open to the air contains the transducer.

A heater, thermostat and stirring pump maintain the water-bath at a constant temperature (Barcroft and Edholm, 1943). The circulation of the water must not cause fluctuations in the level of the water in the recording tube containing the transducer.

The sleeve or glove must fit well so that the total increase in organ volume is transmitted to the recording tube.

Well fitting support must be supplied at the junction of the sleeve or glove with the water-bath to prevent stretching of the sleeve or glove accommodating part of the volume of water displaced.

The Apparatus: Detail

(See Figures I to V)

1. Fore-arm Water-Bath Plethysmograph

The water-bath plethysmograph consists of a clear perspex cylinder into which a poly-vinyl chloride sleeve is fitted to cover the fore-arm. The cylinder measures 6.5 inches in length and 5.5 inches in diameter. It is mounted on a stand.

The top of the cylinder is pierced by three perspex tubes. The central tube, 3.75 inches tall, is of 1.25 inches internal diameter (Lewis and Grant, 1925; Abramson, Zazeala and Marrus, 1939a; Dahn, 1964) and contains the transducer. The outer tubes are 0.75 inches in diameter and are used for fitting the apparatus before being sealed by the calibrating syringe and a Centigrade thermometer.

Water at a constant temperature (32°C.) is exchanged through the plethysmograph via an inlet tube of 0.75 inches internal diameter attached to a baffle near the top of the main cylinder and an outlet tube of the same diameter near the bottom. The apparatus can be emptied by a tap in the inlet tube.

A prefabricated plethysmograph sleeve is used consisting of light-weight poly-vinyl choride, 9.25 inches long, sealed to heavier weight poly-vinyl chloride flanges. The flanges are gripped between pairs of O-rings, greased lightly with petroleum jelly and screwed into the ends of the perspex cylinder to provide a water-tight joint.

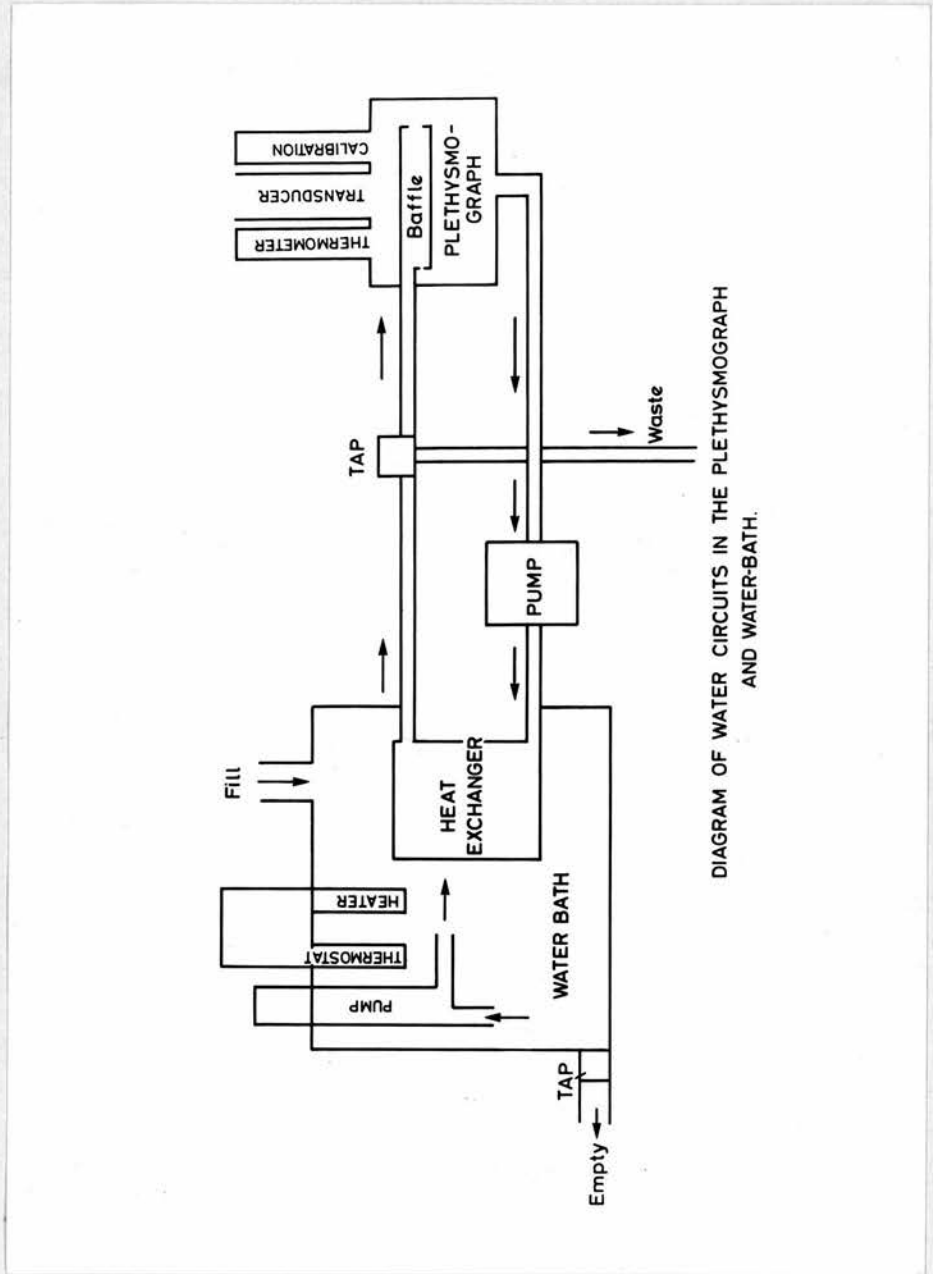



Figure I

Diagram of water circuits in the plethysmograph and water bath.

Figure II

Fore-arm water bath plethysmograph, M.R.C. model. The original apparatus showing the plethysmograph surrounded by the temperature controlling unit.

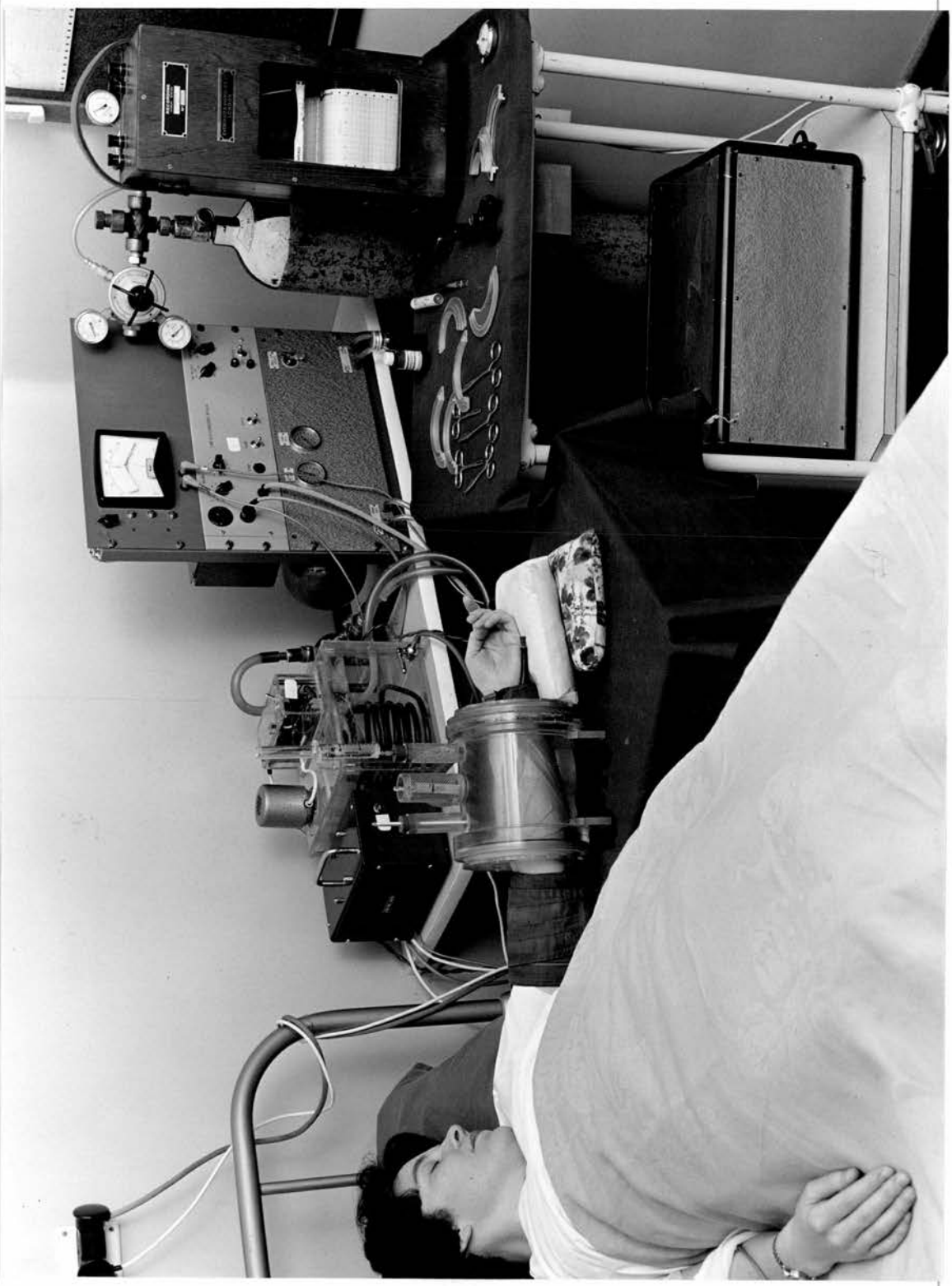


Figure III

Fore-arm water bath plethysmograph. An intermediate stage in the development of the apparatus.

A = Pump circulating water to plethysmograph.

B = Thermostat.

C = Heating element.

D = Stirrer pump.

E = Thermometer.

F = Calibrating syringe.

G = Transducer.

H = Baffle.

I = Movable hand rest.

J = Glove.

K = To empty.

L = Copper heat exchange coil.

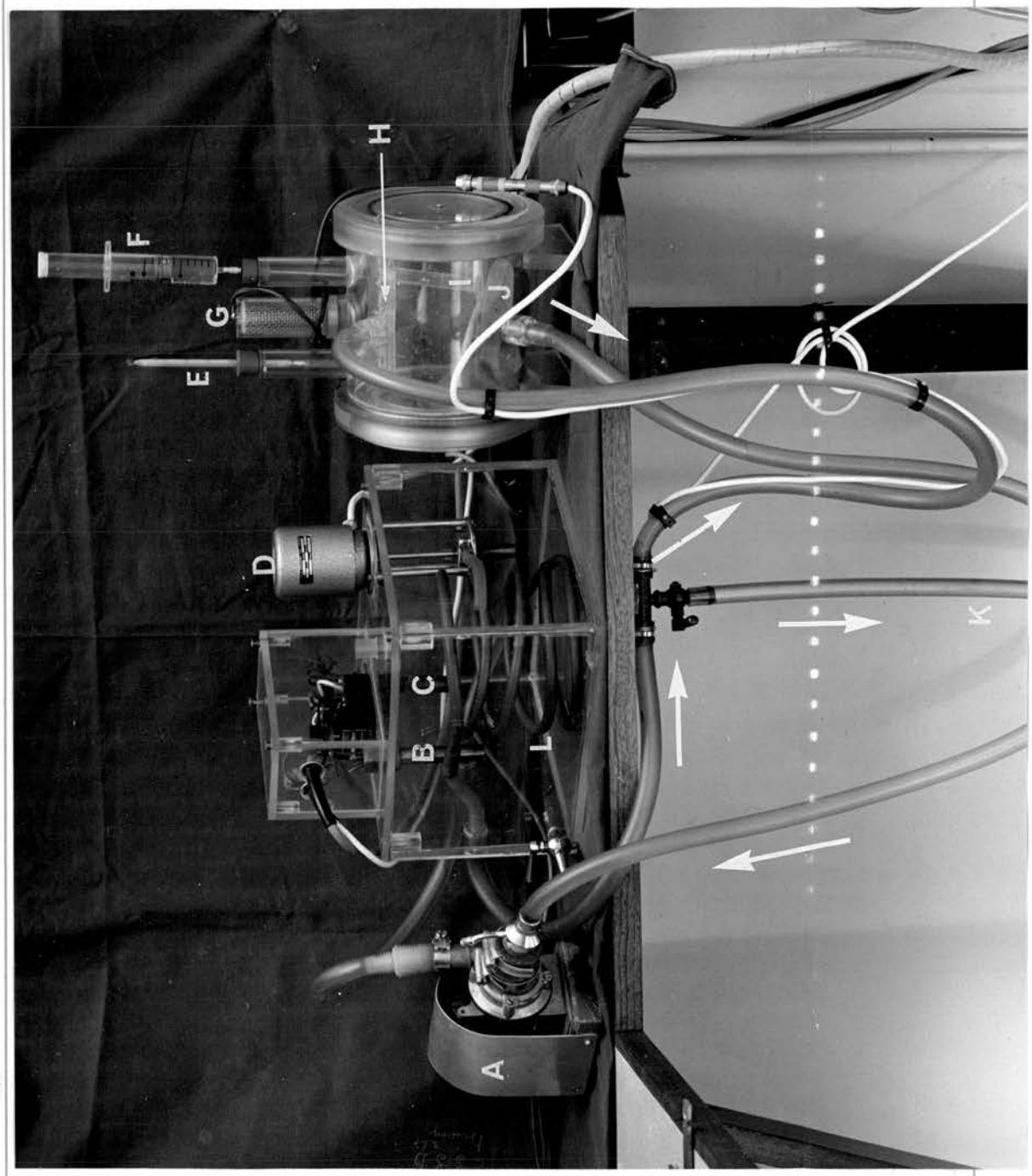



Figure IV

Fore-arm or hand water bath plethysmograph. Detail of final apparatus.

Figure V

Fore-arm and hand plethysmograph. Final apparatus in situ.

The diameter of the sleeve is 3.5 inches at the proximal end tapering to 3.0 inches at the distal end.

2. Hand water-bath plethysmograph

This is adapted from the fore-arm model by replacement of the fore-arm sleeve by a number $8\frac{1}{2}$ surgical rubber glove. The wrist of the glove is clamped between greased perspex O-rings and screwed into place in the main cylinder. The opposite end of the cylinder is sealed by a solid plate of perspex fitted with a handle which serves as a hand rest and which can be rotated by the subject to a position of comfort.

Fitting the Plethysmograph

After the plethysmographs have been fitted over the fore-arm and hand the sides of the sleeve and the wrists of the glove are supported and a good fit obtained by means of pairs of semi-circular perspex formers shaped to fit the limb snugly without compression. They are held in place by O-rings which screw into the main cylinder.

Water Temperature Regulation

A low-voltage water heater and thermostat, which are mains-isolated, are mounted in a clear perspex water-bath containing a copper coil heat-exchanger which is connected via an external constant flow mains-isolated water pump to the inlet and outlet of the plethysmograph. The thermostat is set to maintain the temperature of the water in the plethysmograph at $32^{\circ}$ C. An internal pump circulates the water in the bath. Thus, there are two separate water circulating systems as shown in the diagram (Fig. I). The pump circulating the water through the plethysmograph is isolated from the mains by a low-voltage isolating transformer.

Development of the Apparatus

At first the apparatus was copied from that used in the Division of Human Physiology of the Medical Research Council. In this form the plethysmograph was built into the water-bath containing the temperature regulating mechanism (Fig. II ). Later, a new model was made in which the two components were separated. This made the apparatus more manoeuvrable, easier to manufacture and most of the electrical wiring could be housed further away from the patient. The water temperature regulating mechanism and attendant circuitry was placed on a wall shelf and the heat-exchanger connected to the plethysmograph by lengths of pressure tubing. A more powerful water pump was necessary to maintain a constant flow through this longer circuit. No recordable transmission of vibrations from the pump occurred along this tubing.

The Transducer

The transducer consists of a cylinder of stainless steel gauze and a central stainless steel rod separated by a plastic insulator. The gauze cylinder fits snugly into the central perspex tube in the top of the plethysmograph.

The transducer is connected to a bridge measuring circuit, the central probe forming one of the arms of the bridge (see Circuit diagram, Fig. VI ). The detector, D., is a phase sensitive rectifier used to exclude capacitance effect. As the water level alters in the plethysmograph the resistance in the transducer varies. The output from the phase sensitive rectifier is fed via a variable attenuator, A, to one channel of a two-channel potentiometric recorder, R.

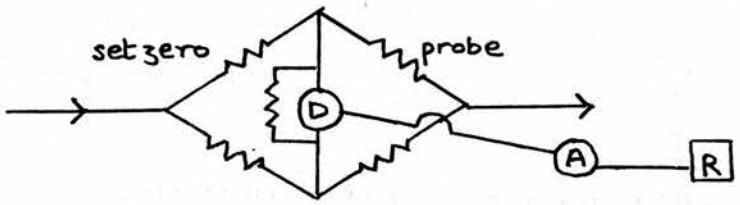



Figure VI

Full details of the circuitry and apparatus, including manufacturers, are found in the appendix.

Arterial and Venous Occlusion

In the original apparatus both arterial and venous occlusion was attained by inflation of sphygmomanometer cuffs by foot pumps connected to glass air-reservoirs. Inflation and deflation of the cuffs were performed manually by means of glass taps connected to mercury manometers which measured the air-pressures in the cuffs.

The periods of inflation and deflation were measured by a stop-watch. This method was changed and automation introduced.

Automatic Inflation of the Venous Occlusion Cuffs

A venous occlusion cuff on each arm is inflated and deflated simultaneously when both hand and fore-arm flows are being measured.

The occlusion cuffs are inflated from a compressed air cylinder fitted with two pressure reducing regulators by means of which the desired pressures can be pre-set to levels indicated by two manometers. One of the pressure reducing regulators is connected to the arterial occlusion cuff on the wrist when fore-arm flows are being measured. The inflation and deflation of this cuff is operated by an on-off glass tap. The other pressure reducing regulator is connected to the venous occlusion cuffs via a copper air-reservoir.

The timing cycle for the venous occlusion cuffs is controlled by a standard astable multivibrator with variable feed-back capacitors

to give pre-set inflation and deflation times which are variable in intervals of 5 seconds up to 20 seconds. The signal from the astable multivibrator is amplified and fed to a solenoid operated air valve (see Appendix for circuit diagram). The circuit may be held in the inflated or deflated positions to allow setting up of the apparatus.

Occlusion Cuffs

(a) Fore-arm flow measurement.

A 6 inch wide sphygmomanometer cuff is used for venous occlusion of the arm just proximal to the fore-arm plethysmograph, and held firmly in place to maintain the preselected inflation pressure and to prevent any movement of the arm occurring as inflation and deflation occur. The inflation pressure selected is 5 mm. Hg. or less below the diastolic level (Lewis and Grant, 1925; Abramson et al, 1939(a); Landown and Katz, 1942; Allwood, 1956).

A 1¾ inch wide cuff is used for occlusion of blood flow to the hand. It is similarly held firmly in place just distal to the plethysmograph. The inflation pressure is usually between 200 and 220 mm. Hg. but may be raised until no pulse can be felt distal to the cuff.

(b) Hand flow measurement.

A 1¾ inch wide cuff is placed just proximal to the hand plethysmograph and similarly kept firmly in position to maintain the inflation pressure and to prevent movement of the hand as inflation and deflation occur. The inflation pressure is the same as that for the fore-arm flow measurement.

The Recorder

A single channel Everard and Vignoles recorder and an amplifier were used originally. When arm and hand flows were measured simultaneously an Elliott twin channel potentiometric recorder replaced both recorder and amplifier.

Calibration

Calibration of the apparatus is made by introducing 10 mls. of water directly into the plethysmograph via a graduated syringe held in one of the outlet tubes in the top of the plethysmograph. Two or three calibrations are made before each series of readings is taken.

Temperature Monitoring

Three thermistor thermometers for monitoring skin and water temperatures are connected to a bridge circuit to give linear current change with temperature.

Setting-up of the Apparatus

1. Position of the Patient

The patient lies comfortably supine on a bed with arms supported at cardiac level (Lewis and Grant, 1925) and abducted 45 degrees. A padded trough shaped perspex support is used for immobilising the arm from the wrist to above the elbow when the hand plethysmograph is used.

2. Position of the Plethysmographs

(a) The Fore-arm Plethysmograph

This is applied to the upper part of the fore-arm to enclose as much muscle and as little skin and bone as possible. Grant and Pearson (1938) estimated, by means of X-rays, that at this level 85% of the limb volume enclosed consisted of muscle, 5 - 8% consisted of bone and 7 - 11% of skin and subcutaneous tissue.

(b) The Hand Plethysmograph

This is positioned to enclose the hand as far as the distal ends of the radius and ulnar.

3. Position of the Occlusion Cuffs

See Page 26.

4. Occlusion Cuff Pressures

See Page 26.

5. Fitting of the Plethysmograph

The semi-circular perspex formers to support the ends of the plethysmograph sleeve and glove are selected to fit each individual, without compression of the limb, and are screwed into place.

6. Filling of the Plethysmograph

When not in use the plethysmograph is left half filled with water to prevent air being sucked into the system. Filling is completed when the plethysmograph is in the correct position on the limb and the supports are in place. Care is taken that no air bubbles are trapped in the apparatus. The water temperature is $32^{o}C$. The water-level in the transducer tube is adjusted by means of a syringe to obtain the base line in the tracing.

7. Site of the Thermistor Thermometers.

Thermometers are placed between the plethysmograph sleeve and the anterior surface of the fore-arm and between the glove and the palm of the hand and on the anterior surface of the free-fore-arm. The latter is insulated from draught by several layers of gauze and held in place by an elastic bandage. Flow readings are not taken until the thermometer readings are steady.

8. Selection of Cuff Inflation-Deflation Times

Timing is selected to give 5 second inflation and 10 second deflation. The former is ample to give a good tracing of the initial increase in volume before the character of the tracing is altered by the build-up of pressure in the distending veins.

The arterial occlusion cuff on the wrist distal to the fore-arm plethysmograph is inflated for three minutes while readings of fore-arm flow are obtained (Kerslake, 1949).

9. Method of Recording

When the patient has been lying comfortably for three-quarters of an hour and pulse and temperature recordings are stable the simultaneous recording of hand and fore-arm flows is started. The fore-arm arterial occlusion cuff is inflated as the stop-watch is started. The base-line of the tracing is adjusted by altering the water-level in the transducer tube and two or three 10 ml. calibrations are made as previously described. The automatic inflation and deflation of the venous occlusion cuffs is started. At the end of three minutes all cuffs are deflated. Two or three further series of recordings are made at intervals of three minutes. In this way between 20 and 30 separate recordings of blood flow are available for measurement. Kerslake (1949) stressed that distal arterial occlusion should be maintained throughout the recording of fore-arm flow rates and that one minute should elapse before the first fore-arm recording is made. In this study the time was used to adjust the base-line oftthe recording and to obtain reproducible calibrations. Also, the first two fore-arm flow rate readings obtained thereafter were discarded.

Artefacts

Artefacts may occur from various factors.

1. Rhythmic deflections on the base line due to transmission of movement from respiration. These may be removed from the tracing by immobilising the limb either by increasing or adjusting the limb support by cushions or sandbags.

2. Sudden deflection of the base line at inflation of the cuff. A similar deflection may occur in the tracing synchronous with the deflation of the cuff. These deflections are due to movement of the cuff displacing the limb in the water bath and can be eliminated by resiting the cuff and by bandaging it firmly to minimise the volume increase in the cuff on inflation.

3. Gradually rising base line can be due to incomplete emptying of the veins after deflation of the cuff. It is important to ensure that the apparatus is not compressing the limb in any way.

4. Gradually decreasing base-line can be due to the release of air bubbles which have hitherto been trapped in the apparatus, or to air being allowed to enter or to a leak in the system.

5. Irregular deflections can be due to movement of the patient, voluntary or involuntary, or due to electrical interference.

6. Regular small deflections due to pulse validate the sensitivity of the apparatus and are used for selection of the area of the curve to be read (see method of interpretation of tracing).

Variations in Flow Rates

Variations in the rate of blood flow were first noted by Harvey (1628) who states "Meanwhile this much I know, and may I remind all men of it, that the blood makes the passage at times in greater, at times in lesser,amount; and that its circuit is effected now more

rapidly and now more slowly according to temperature, age, external and internal causes, things natural and non-natural, sleep, rest, feeding, exercises, mental affections, and the like."

Numerous workers have shown variations in flow rate with changes in environmental and local temperature. The references are not enumerated here but are discussed later. A comprehensive summary is given in Physiology of the Circulation in Human Limbs in Health and Disease by Shepherd (1963). For this reason both water bath and room temperature were maintained at constant levels. Spontaneous fluctuations, however, occur even at constant temperature; Abramson etaal, 1939; Cooper et al, 1955.

Sleep may also alter blood flow rates. A decrease in flow was noted by Abramson et al, 1939a. The effect of emotional stress has been shown to increase blood flow rates by Grant et al, 1938; Abramson et al, 1939a; Abramson et al, 1940; Wilkins et al, 1941; Hickam et al, 1948; Allwood et al, 1959. Blair et al, 1959, and Fencl et al, 1959 showed that the increase in flow rate due to stress occurred in the muscle vessels and Barcroft et al, 1960 attributed this to both humoral and nervous factors. Vanderhoof et al, 1962, studying normal and psychiatric patients showed that repetition of the stress eventually extinguished the response. Differences in flow rates between the two sides of the body have been shown by Greenfield et al, 1951; Duff, 1956; and Hyman et al, 1963. The difference is about 3 per cent. The effect of posture has been demonstrated by many workers; in the present context those described by Brigden et al, 1950, and Roddie and Shepherd, 1956, are most relevant.

For these reasons conditions under which readings were made were strictly controlled and are descibred in the chapter on the Design of the Experiment.

Undue variations in mean flow rates for each three minute series of recordings are sometimes found. When this occurs the patient is left to rest for a longer period, and the apparatus is checked for factors which may produce artefacts. In the case of the patient being investigated for the first time the first series of recordings is used as a trial run to demonstrate the method to the patient and is afterwards discarded.

The Measurement of Arm and Hand Volume

Lines were drawn on the limb delineating the area contained in the plethysmograph. The limb volume was simply measured by water displacement in a large perspex cylinder.

The Record

Part of a typical recording is shown in Figure VII.

The measurement of flow rates from the recordings were made as described in The Appendix of Sympathetic Control of Human Blood Vessels by H. Barcroft and H.J.C. Swan, Arnold, 1953.

For accuracy measurement must be made over the early part of the recording before back-pressure shows an effect and in practice a straight line is drawn through the first three pulse deflections on the curve. An experimental constant, D, is calculated for each series of recordings from the formula $D = \frac{XV}{M}$ where X is the vertical distance travelled by the recorder writing point for 1 ml. increment of content, V is the volume of the limb in hundreds of mls. and M is the distance in centimetres travelled by the paper in 1 minute. The upward movement of the writing point in centimetres while the

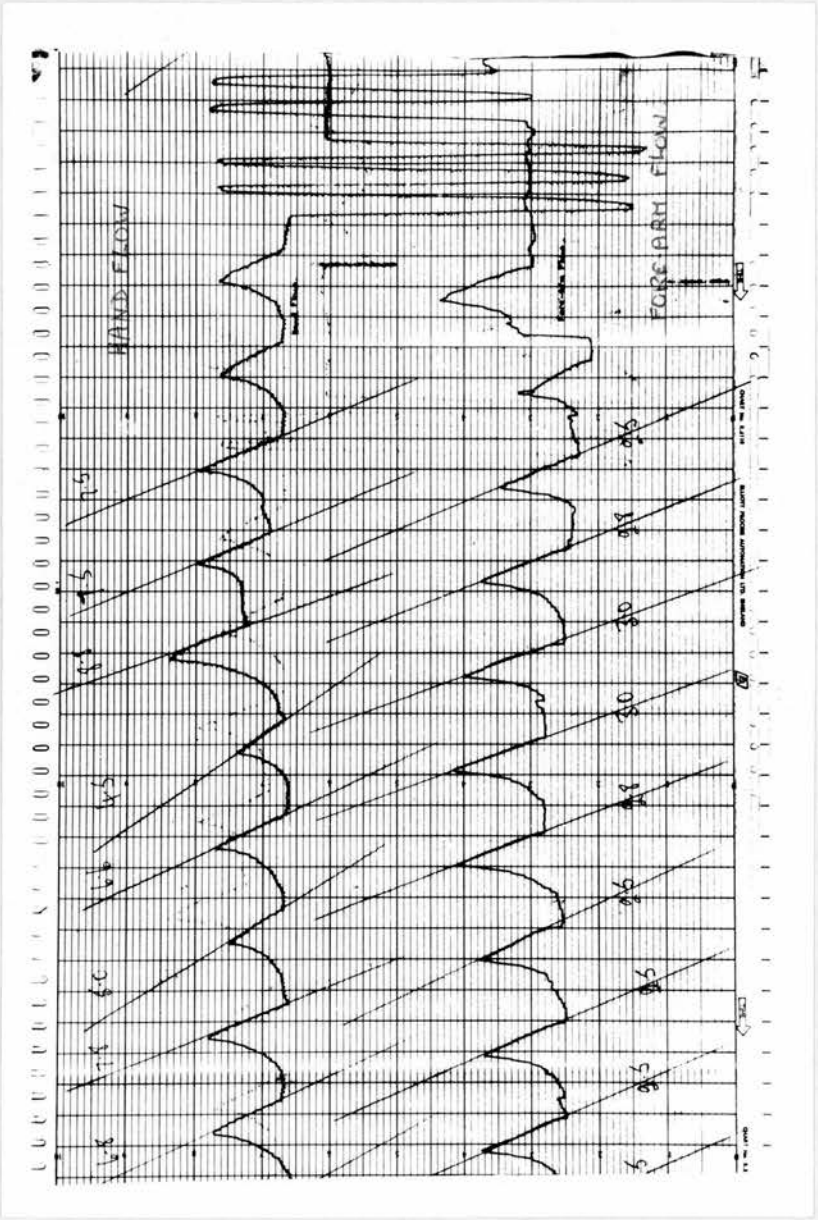



Figure VII

Sample Tracing

paper travels D centimetres is the rate of blood flow in mls. per 100 mls. of tissue per minute (F in the diagram). The proof of this formula is given in the monograph of Barcroft and Swan (1953).

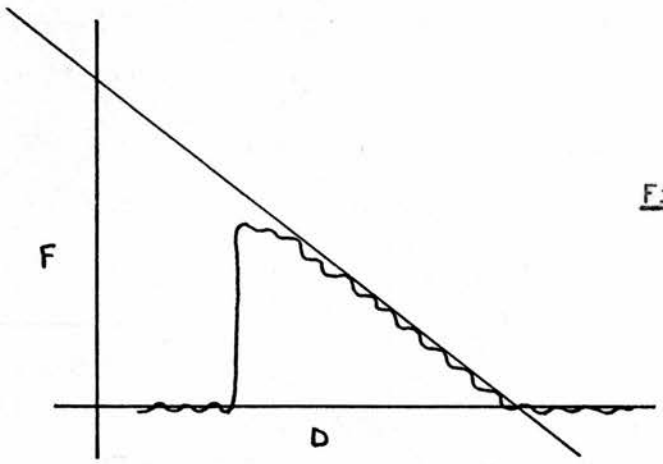



Figure VIII

Values for F are simply obtained using a set square calibrated in centimetres. For the measured distance D in centimetres F can be read from the point where the hypotenuse crosses the F axis.

To save time in the calculations, tables of D were prepared by computer for varying values of X and V divided by the constant M by Miss A. C. Bramley formerly of the Medical Research Council Computer Services Centre.

The mean of the values obtained during each recording session for each subject was calculated.

## Validity of the Method

### Experiment to Test the Accuracy of Calibration of the Plethysmograph

The plethysmograph is calibrated by means of injecting and withdrawing a known amount of water into the water-bath surrounding the limb and measuring the deflection obtained in the recording.

A mean of two to three readings is taken.

A direct method of calibrating the apparatus is to inject a known amount of fluid into a vein and to measure the deflection produced.

Tests were carried out on four non-pregnant subjects.

The fore-arm apparatus was set up in the usual way with the inflation cuffs very close the ends of the plethysmograph. An Intracath was inserted into a vein on the back of the hand and threaded upwards until the tip of the catheter just protruded proximal to the distal occlusion cuff. It was then connected via a three-way tap to a bottle of normal saline and a glass syringe in the usual way. The patient was allowed to rest.

The proximal and distal cuffs were inflated to occlude all flow in the segment of the arm in the plethysmograph, i.e. to between 240 and 250 mm. Hg. The saline was injected slowly into the vein in 2ml. increments until 8 to 10 mls. had been injected. Some discomfort was felt in the veins were overdistended and this limited the amount which was injected. The saline was then removed in 2 ml. increments. The cuffs were deflated and the plethysmograph calibrated in 2 ml. increments by means of the syringe in the water bath. Alternate calibration by intravenous route and water bath route was repeated several times for each subject.

The results obtained, together with the expected and best straight lines,are shown in the graph ( Figure IX ). For the best straight line obtained from the data b = 1.051, giving a mean deflection of 10.566 centrimetres for the syringe calibration compared with a mean deflection of 10.0 centimetres for the intravenous calibration; an error of 5.66 per cent. This would givenan overestimation of the flow rate by a mean of 5.66 per cent.

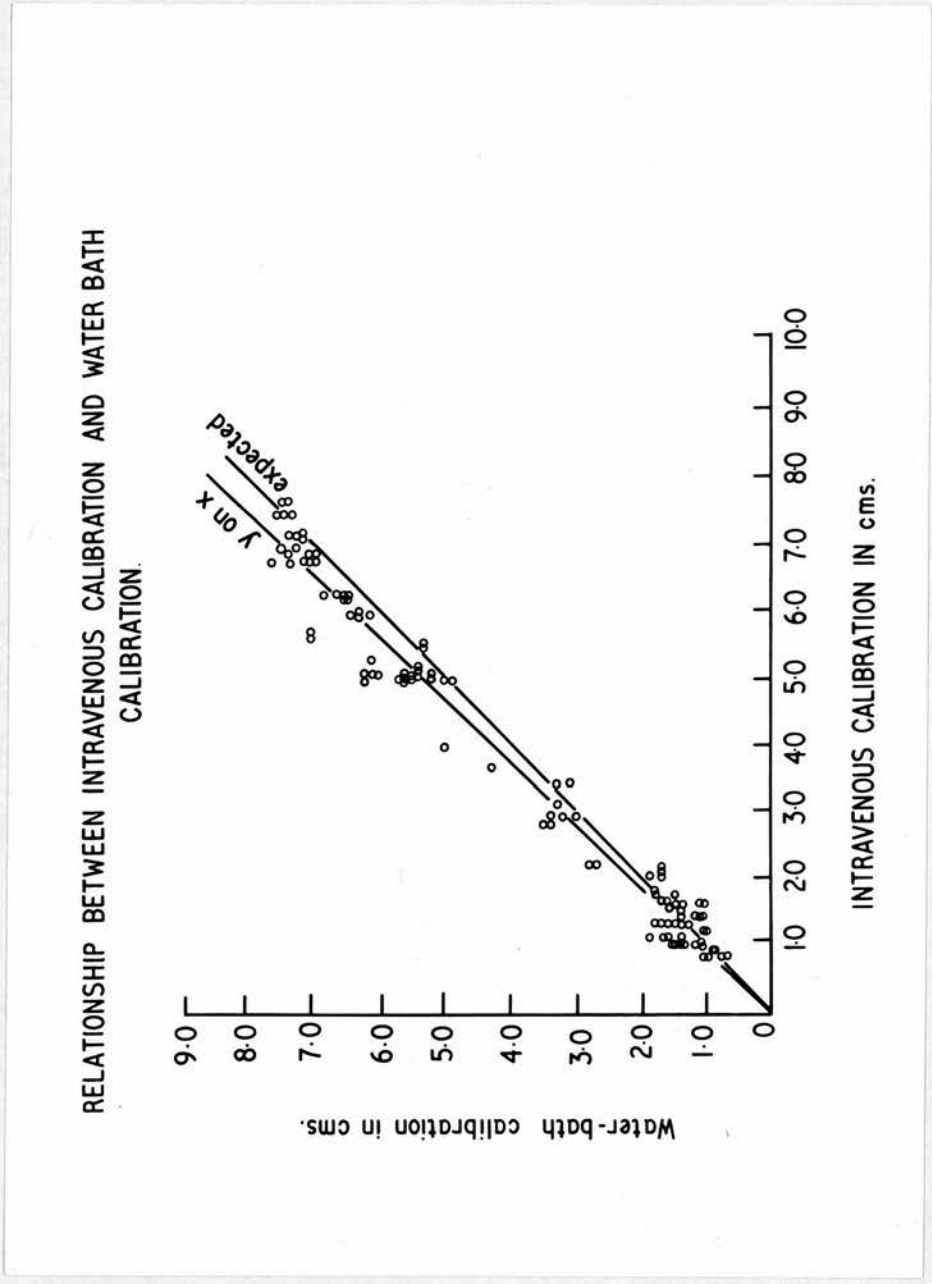



Figure IX

Relationship between intravenous calibration and water-bath calibration.
Note:
The disparity between the two methods of calibration is slightly exaggerated in this diagram owing to the difficulty of representing many points which were either very close together or reproduced each other exactly. Some of the latter points had to be omitted.

## The Design of the Experiment

### The Subjects

Control non-pregnant subjects were selected from the Hospital staff. They were within the age range of the pregnant subjects, healthy and not taking oral progestogens.

Patients who were not more than 11 weeks pregnant were selected from the Ante-Natal Booking Clinics. The subjects were clinically normotensive, free from cardiovascular disease and without history of hypertension or ante-partum haemorrhage. For these reasons the subjects were mainly primiparous. The multiparous patients in the study were accepted for hospital confinement on social grounds only.

Patients who book early for hospital confinement are in a minority and those who are accepted frequently fall into high-risk groups. As suitable subjects were difficult to obtain contact was made with local General Practitioners who were very helpful in providing patients in early pregnancy who would not normally be accepted for hospital confinement.

Four of the subjects were of West African origin and the remainder were white Europeans. All social grades were included in the study.

### Obstetric Care

All antenatal and post-natal care and the delivery of each subject was supervised by myself and my midwife assistant who also helped with the plethysmography. Thus, there was complete continuity of care. Every effort was made to allay any anxieties the patient may have had before flow measurements were made.

Advice to Subjects

The patients were advised to have a very light meal at least two hours before arriving at the hospital and to refrain from violent exertion on the way.

The Environment

Flow measurements were made in an air-conditioned room maintained at 21 to 22°C. and all efforts were made to exclude extraneous noise. The subjects rested in this environment for 40 minutes before flow readings were made.

Subjects were examined on the same day of the week and the same hour of the day throughout.

Position of the Patient and Side of the Body Examined

All measurements were made with the patient supine in a comfortable bed with her head and neck raised on two pillows. All forearm flow measurements were carried out on the left arm and all hand flow measurements were carried out on the right hand.

Anaemia Prophylaxis and Therapy

All subjects were given Ferrous gluconate to be taken once daily prophylactically. The dose was increased to thrice daily for treatment of anaemia of 75% and below. A few patients required parenteral iron therapy and folic acid, 5 mg., daily was given to subjects with megaloblastic anaemia after a prophylactic dose of 1,000 µg. of vitamin B12.

Diet

A weight gain of 2 lbs. or more per week was considered excessive and when this occurred patients were requested to diminish their carbohydrate intake. When clinical oedema occurred a low salt diet was recommended.

Experimental Intervals

Blood flow rates were measured in each subject at four-weekly intervals until term, on the third day, and at 6, 12 and 40 weeks after delivery. Between twenty and thirty separate readings of the flow rate were made at each visit over a period of twenty minutes. Each patient had measurements made on seven to nine occasions before delivery and two to four occasions after delivery. It was found that to study one patient completely took fifteen to sixteen months.

It was not always possible to obtain measurements for the last two intervals (36 - 39 weeks and 40 - 43 weeks gestation) because of the onset of labour. As plethysmography requires absolute stillness on the pa t of the patient, readings could not be obtained in labour. It was not always possible to follow patients for long after delivery owing to distant removal, emigration or further pregnancy.

## Other Parameters Measured at the time of Flow Measurement

1. Bodyweight

All subjects were weighed wearing only the light gown provided and the same scales were used throughout.

2. Blood Pressure

The blood pressure was recorded when the patient had been resting quietly for ten minutes. The diastolic level was taken as the point where the Korotkoff sounds became muffled. No correction was made for the thickness of the arm.

3. Pulse Rate

The pulse rate was measured over one minute from the radial artery when the patient had been resting quietly for ten minutes and was monitored during the experiment by means of the deflections obtained in the recording.

4. Oral Temperature

The oral temperature was measured over two minutes with a mercury thermometer,

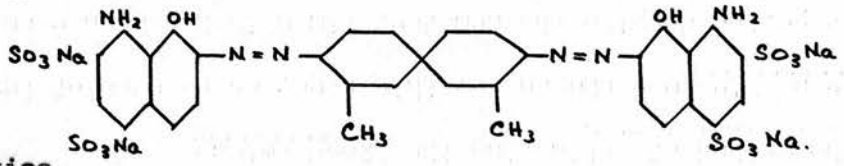
5. Fore-Arm Skin Temperature

This was monitored throught the experiment with a thermistor thermometer as previously described on Page 28.

6. The Method of Estimating the Blood Volume

Evans Blue was chosen for this study as no case of toxicity has been reported despite the numerous times it has been used since Dawson, Evans and Whipple first introduced it in 1920. It was supplied by General Diagnostics Division of Warner-Chilcott, Morris Plains, New Jersey as Evans Blue Injection, U.S.P. (T-1824) in a

0.5% aqueous solution, equivalent to a 0.452% anhydrous salt. It is a tetrasodium salt of 4,4'-Bis [7-(1-amino-8-hydroxy-2,4-disulpho-naphthylazo]-3,3'-bitolyl and has the following formula:-




Properties

The dye is soluble in water, saline and alcohol. It combines with plasma albumin according to Ogston in a personal communication to Courtice (1943) and does not diffuse into blood corpuscles (Courtice, 1943).

The optical density is directly proportional to its concentration and maximal spectral absorption of the dye in plasma occurs at 620 mμ - 625 mμ at which spectral absorption of haemoglobin is negligible. Hence minor degrees of haemolysis do not invalidate its measurement (Gregerson et al, 1935).

Evans Blue can be extracted from plasma by various methods. That of Clausen and Lifsen (1956) was found most suitable and they claim recovery rates of 95 to 100%.

Evans Blue is stable in aqueous solution, and is not affected by light. When stored as a standard aqueous solution at $4^{o}$C. no deterioration was found over periods up to 6 months, identical optical density readings being obtained during this time.

Distribution, Metabolism and Excretion of Evans Blue

Evans Blue disappears very slowly from the blood, substantial quantities still being present 24 hours after injection. From 16 hours after injection the dye disappears at the rate of 2.2% per hour (Gibson and Evans, 1937) or 5 - 8% per hour (Gregerson et al, 1935) but variations are noted between subjects (Courtice, 1943).

In animal experiments Evans Blue has been extracted from the thoracic duct and cervical duct lymph by 15 minutes after injection. The amount increases during the first hour (Courtice, 1943; Ferrebee, Leigh and Berliner, 1941) but only about 0.5% of the total injection ever appears in lymphatics. The dye is mainly removed from the blood stream by phagocytosis and removed to the reticulo-endothelial system (Gibson and Evans, 1937) and metabolised chiefly in the liver (Fouts et al, 1957). Gibson and Evans state that it is not found unchanged in the urine of patients with normal kidneys. They could not detect dye in oedema fluid, pleural or ascitic fluids or cerebro-spinal fluid. Evans Blue could not be found in foetal cord blood, amniotic fluid or placental membranes, when the patient had been injected with the dye shortly before delivery, by either Gibson and Evans (1937) or Thomson et al (1938).

Toxicity

Gibson and Gregerson (1935) injected up to 20 mg./Kg. bodyweight into growing rats without side-effect. This dosage is far higher than any given to adults, the recommended dose being 0.35 mg./Kg. bodyweight. In the present study 0.2 mg./Kg bodyweight and less was used successfully.

A transient staining of the skin was seen in a few patients.

In Vitro Decay

No change was found in optical density in standard solutions kept for up to 6 months in a domestic refrigerator. Nor was any change found in plasma extracts kept for up to 6 weeks under the same conditions.

In Vivo Decay

Although dye could still be recovered 24 hours after injection

according to Gibson and Evans, no evidence of dye was found in plasma samples taken from 3 to 7 days after the last injection.

Mixing Time

Courtice found mixing to be complete in 6 minutes, Gibson and Evans found 7.5 minutes to be the mean mixing time in the normal adult human with shorter times in hyperthyroid states. The latter workers could find no difference in mixing times in the pregnant state. After ten minutes the dye disappears extremely slowly from the circulation and reproducible results are obtainable for two hours or more.

Extraction of Evans Blue from Blood

Extraction was carried out using the method of Clausen and Lifson (1956). Slight modifications were made to this extraction method (Walters, 1964).

Six millilitre samples of venous blood are withdrawn into tubes containing a small amount of powdered heparin and centrifuged at 3,000 revolutions per minute for ten minutes. One millilitre of plasma is withdrawn and 2 mls. saturated urea solution, 4 mls. of pure acetone, 0.5 mls. 10% Zinc sulphate and 0.5 mls. of 0.5 N sodium hydroxide are added successively. To prevent turbidity occurring the last two additions must be standardised against each other by titration to a phenol-phithalein end point. Between each addition of reagent the tube is thoroughly shaken and finally centrifuged for 15 minutes at 3,000 revolutions per minute. The supernatant fluid is transferred to a second clean, dry tube by a Pasteur pipette avoiding the lipoid material. The supernatant fluid is centrifuged for a further 15 minutes at 3,000 revolutions per minute. Evaporation is avoided by waxed paper caps firmly applied to the tubes.

Turbidity in the final extract can be produced if the Zinc sulphate and sodium hydroxide deteriorate causing changes in pH. They must be retitrated every week. Contamination with detergent can also cause turbidity. All glassware has to be thoroughly cleaned and well rinsed with distilled water before drying.

The optical density of the final supernatant extract is measured in a Unicam S.P. 500 spectrophotometer at 620 mμ wavelength and slit 0.02 mm. against blanks prepared from pre-injection plasma and distilled water. The standard solution is prepared by adding 0.02 mls. of the same batch of 5% Evans Blue by micro-syringe to 50 mls. distilled water. The mean of two readings of each is taken.

Recovery of Evans Blue from Plasma

A standard solution was prepared as before and 0.02 mls. Evans Blue was added by micro-syringe to plasma to make equivalent concentration and extracted as before. The recovery rates are given in Table 1 and are corrected for dilution.

As can be seen from the Table a little variation was found in the readings of optical density of the samples of aqueous standard during each reading session. In almost every case there was a loss in recovery of the dye from plasma compared with the aqueous solution. The mean error was -2.932%.

Recovery of Evans Blue from Plasma Extraction

| | Optical Density | | Error | % Recovery |
|---|---|---|---|---|
| | Standard in water | Standard in plasma | | |
| Day 1 | 0.660 | 0.720 | +0.06 | 109.1 |
| | 0.660 | 0.720 | +0.06 | 109.1 |
| | 0.660 | 0.740 | +0.08 | 112.1 |
| Day 2 | 0.640 | 0.580 | -0.06 | 89.8 |
| | 0.632 | 0.560 | -0.072 | 88.6 |
| | 0.664 | 0.640 | -0.024 | 96.4 |
| | 0.656 | 0.660 | +0.004 | 100.6 |
| | 0.664 | 0.640 | -0.024 | 96.4 |
| | 0.656 | 0.620 | -0.036 | 94.5 |
| | 0.640 | 0.620 | -0.020 | 96.9 |
| Day 3 | 0.640 | 0.600 | -0.040 | 93.8 |
| | 0.660 | 0.640 | -0.020 | 97.0 |
| | 0.640 | 0.620 | -0.020 | 96.9 |
| | 0.632 | 0.600 | -0.032 | 94.9 |
| | 0.640 | 0.600 | -0.040 | 93.8 |
| | 0.640 | 0.580 | -0.060 | 90.6 |
| | 0.632 | 0.560 | -0.072 | 88.6 |
| Mean | 0.648 | | -0.019 | 97.00 |
| S.D. | 0.012 | | 0.046 | 7.07 |
| S.E. | 0.003 | | 0.011 | 1.71 |
| Error | | | -2.932% | |

Table 1

Method of Blood Volume Estimation

As emotional disturbance has such a profound effect upon the peripheral circulation it was decided to dispense with the method of flushing dye into a vein by an intravenous drip. Evans Blue Dye was drawn up into a 2 ml. syringe and the needle discarded. The plunger of the syringe was drawn back so that air entered the open end of the syringe to avoid loss of dye during transit. The syringe was weighed together with a fresh sterile needle. This needle was attached to a collecting syringe and used to obtain between 8 and 10 mls. of blood from the left ante-cubital vein after release of venous occlusion. The syringe was then detached and an assistant emptied the blood into a bottle containing dried heparin. The plunger of the Evans Blue syringe was carefully adjusted to exclude air without loss of dye and attached to the needle in the vein and the injection made over one minute. At the end of the injection the syringe and needle were removed and reweighed together. The total weight of the dye injected was obtained by subtracting the two weights. In this way the dye remaining in the bore of the needle is accounted for. Ten minutes after injection of dye, as timed by a stop-watch, an 8 - 10 ml. sample of venous blood was collected as described before, from the right ante-cubital vein to avoid possible slight contamination from the previous injection site.

Calculation of Blood Volume

$$\frac{\text{Optical density of standard solution}}{\text{Optical density of patients' plasma}} = \frac{\text{Concentration of dye in standard}}{\text{Concentration of dye in patients' plasma}}$$

The concentration of the standard was $\frac{0.02}{50.00}$ mls.

The concentration of the dye in patient's plasma =

$$\frac{\frac{\text{weight injected}}{\text{specific gravity}}}{\text{plasma volume}} \text{ mls.}$$

The patient's plasma sample is diluted 8 times.

Where ODS = optical density of standard solution

ODP = optical density of patient's plasma

I = weight of dye injected

P = plasma volume

$$P = \frac{ODS}{ODP} \times \frac{I}{1.002} \times \frac{50}{0.02} \times \frac{1}{8}$$

Also $P = \frac{100 - \text{packed cell volume}}{100} \times$ total blood volume.

Therefore total blood volume $= \frac{100}{100 - \text{P.C.V.}} \times P$

No correction is made for the recovery error (2.93%) nor for the dye trapped in the packed cells which is approximately 4% (Gregersób et al, 1935; Gregerson and Schiro, 1938). Similarly, no correction has been made for total body haematocrit as differing values for corrections have been calculated by different workers (Gibson et al, 1946; Carton et al, 1951, Loria et al, 1962; Chaplin et al, 1953; Paintin, 1963) and concurrent studies on total red cell count by radio-active isotopes was not carried out in this study.

7. Haemoglobin, Red Cell Count, Packed Cell Volume, Mean Corpuscular Haemoglobin Concentration, Mean Corpuscular Volume and White Cell Count

Blood from the cubital vein was obtained after occlusion had been released and collected in Sequestrene bottles.

Haemoglobin

The oxyhaemoglobin method was used in which 0.02 mls. of venous blood was washed into 4 mls. of 0.04% ammonia in distilled water. The tube was inverted several times to ensure complete mixing and the solution was read in a Unicam S.P.300 Colorimeter using an Ilford green filter(No.625). The standard used was a neutral grey glass screen with an extinction coefficient of 0.475. With the colorimeter used the standard was equivalent to 14.8 G. haemoglobin per 100 mls. of blood.

Red Cell Count

This was measured in the routine manner using the Thoma-Zeiss Haematocytometer (Hutchinson and Hunter, 1955).

Packed Cell Volume

The micro-haematocrit method was used to measure the packed cell volume. Chaplin and Mollison (1952) regarded the macrohaematocrit method as more reliable but Walters (1964) compared both methods in 30 subjects during serial studies in pregnancy and found the results for each method identical. In this study the haematocrit was measured by the same technician in the same laboratory as that in which Walters study was made.

The Hawksley method was used with equipment from Hawksley & Sons, Ltd. A capillary tube, 7.5 cms. long, with a bore of 0.5 mm. was filled with carefully mixed venous blood and sealed in a bunsen-burner flame. The tube was placed in the Hawksley centrifuge and spun for 5 minutes at 12,000 G. The packed cell volume was measured after placing the tube in a Hawksley haematocrit calculator.

Mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration and mean cell volume were calculated from the foregoing parameters in the usual way (Hutchison and Hunter, 1955).

White cell count was calculated in the routine manner using a Thoma-Zeiss Haematocytometer (Hutchison and Hunter, 1955).

7. Pregnanediol Excretion

Twenty-four or forty-eight hour specimens of urine were collected at monthly intervals during pregnancy from reliable subjects. The pregnanediol excretion was measured by the method of Klopperet al (1955).

8. Cornification Index of Posterior Vaginal Fornix Aspirate

Samples of posterior vaginal fornix aspirate were obtained from each patient at every visit. Two slides were prepared from each sample and stained by the Papanicolaou staining technique. The cornification index and progesterone effects were estimated by Dr. Erica Wachtel as described in her book 'Exfoliative Cytology in Gynaecological Practice,' 1964. The cornification index is calculated by counting the number of cells with pyknotic nuclei present in an unselected sample of 200 cells from each slide and expressing the result as a percentage of the total number of cells counted. The results are inaccurate when severe genital tract infection is present and in these cases the results were discarded for the purposes of this study.

# RESULTS

Fore-Arm Blood Flow Rates

## FORE-ARM BLOOD FLOW RATES

### The Control Group

Subjects

Thirty-two non-pregnant subjects were examined on a total of 152 occasions. The mean age was 26.5 ± S.D. 4.51 and the range 19 to 35 years. One subject had two children; the remainder were nulliparous. The mean height was 65.23 inches ± S.D. 2.27 and the mean weight was 134.79 pounds ± S.D. 16.09. The mean surface area was 1.672 square metres ± S.D. 0.11.

Results

A mean fore-arm flow rate for the group was calculated from the mean flow rates for each subject and was 4.0 mls./100 mls./minute ± S.D. 1.68.

It was found that the mean fore-arm flow rate calculated from the mean flow rate for each patient from the period six weeks to 40 weeks after delivery, was also 4.0 mls./100 mls./minute ± S.D. 1.61.

In the estimation of the effect of some of the parameters on fore-arm blood flow rates, it was therefore considered reasonable to include readings from these patients with those of the control group. Where this has been done the fact is indicated by the number of degrees of freedom.

1. The Effect of Age on Fore-Arm Flow Rates

A significant reduction in flow rate was found with increasing age. The regression line of age on flow rate was calculated, giving $b = -0.073$, $t = 2.049$ on 113 degrees of freedom, $0.05 > P > 0.02$. This

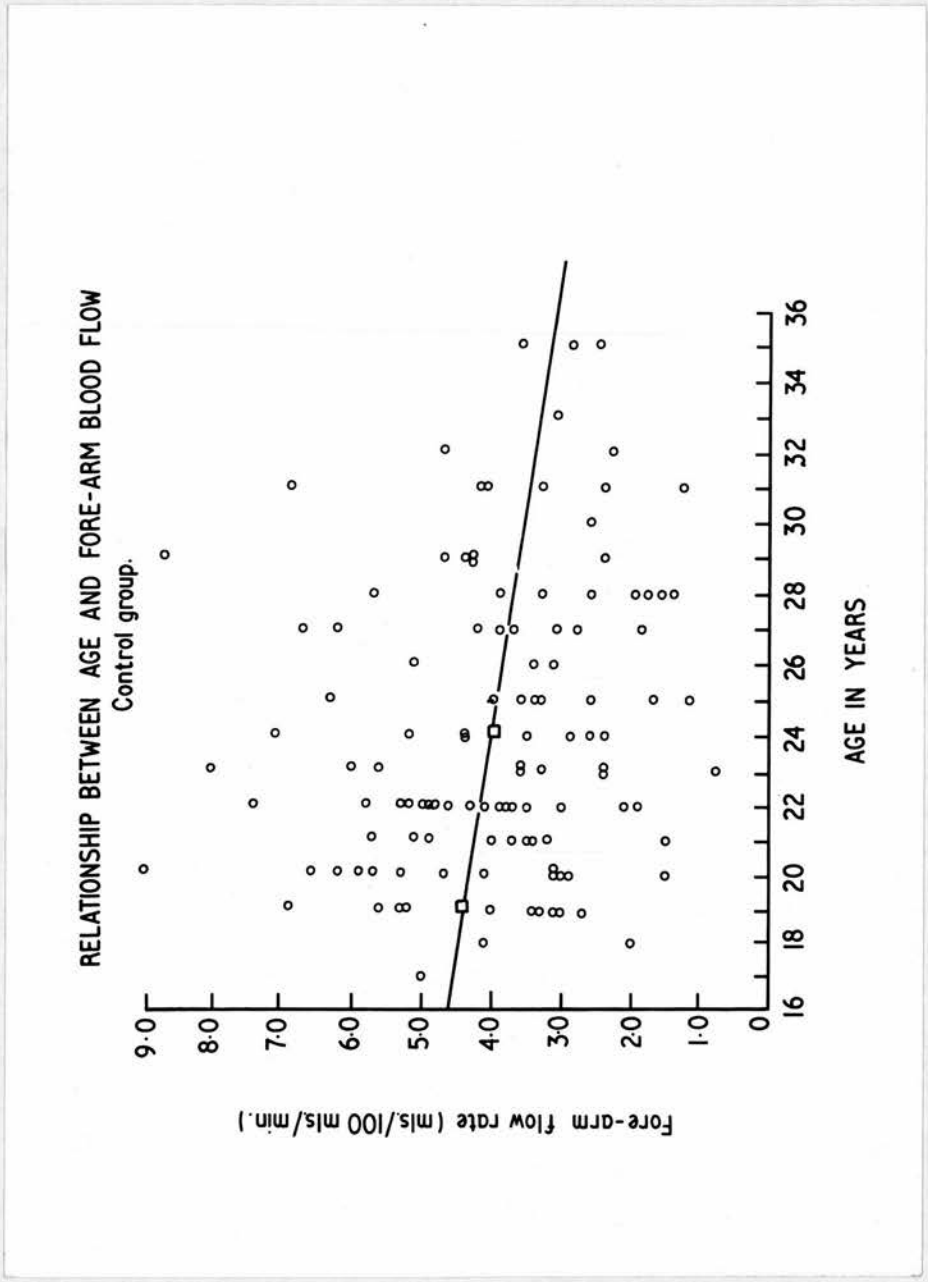



Figure X

Relationship between age and fore-arm blood flow in the control group. The regression line of flow on age is represented by the open squares and continuous line.

gave a mean fore-arm flow rate of 4.4 mls./100 mls./minute at age 19 years, falling to a mean flow rate of 3.2 mls./100 mls./minute at 35 years.

2. Parity and Fore-Arm Flow Rates

The mean fore-arm flow rate for the 31 nulliparous subjects in the control group was 4.0 mls./100 mls./minute which was the same as that for the 83 parous patients.

3. Body Surface Area and Fore-Arm Flow Rates

The surface area for each subject was calculated from her height and weight according to the formula of Dubois and Dubois (1916).

No relationship was demonstrable between surface area and fore-arm flow rates; $t = 0.046$ on 113 degrees of freedom, $P > 0.9$.

4. Smoking and Fore-Arm Blood Flow Rates

Of the 32 non-pregnant control subjects, 11 subjects smoked and 21 subjects did not. The mean fore-arm blood flow rate for the 11 smokers was 4.54 mls./100 mls./minute $\pm$ S.D. 1.91 and that for the non-smokers was 3.67 mls./100 mls./minute $\pm$ S.D. 1.51. There was no significant difference between these means; $t = 1.415$ on 30 degrees of freedom, $0.3 > P > 0.2$.

5. Menstrual Cycle and Fore-Arm Blood Flow

Nineteen non-pregnant subjects were examined in both stages of the menstrual cycle; on 75 occasions in the pre-ovulatory phase and on 60 occasions in the post-ovulatory phase. The mean of the readings in each stage of the cycle was obtained for each patient. These figures gave a mean pre-ovulatory flow rate of 4.2 mls./100 mls. per minute $\pm$ S.D. 1.90 and a mean post-ovulatory flow rate of 3.7 mls. per 100 mls./minute $\pm$ S.D. 1.90. A t-test carried out on the paired

readings of the 19 subjects gave t = 1.511 on 18 degrees of freedom, $0.2 > P > 0.1$.

6. Reproducibility Between Intervals

Thirteen of the thirty two non-pregnant control subjects were examined at four-weekly intervals for seven months. There was no significant difference between the fore-arm flow rates from the first to last intervals. A paired t-test gave t = 1.377 on 12 degrees of freedom, $0.2 > P > 0.1$.

7. Seasonal Effect and Blood Flow Rates

The following data concern the pregnant groups mainly but it is convenient to include it at this point. As blood flow rate estimations were made over periods of up to seventeen months in all the pregnant subjects and some of the non-pregnant subjects, it was possible that fluctuations in flow rate may have been due to seasonal influences. From tables of mean prevailing temperature in London for each month of the year ( Whitakers Almanack, 1968), the six colder months were November to April inclusive and the six warmer months were May to October inclusive. There was no significant difference between the number of occasions patients were examined in cold or warm months; $X^2$ on 2 degrees of freedom was 0.509. Forty patients began their pregnancies in the cold months and 44 in the warm months.

8. Normal Body Temperature and Fore-Arm Blood Flow

No relationship could be demonstrated between mean body temperature over the normal range shown by the patients and the corresponding fore-arm blood flow rate; t = 0.027 on 97 degrees of freedom, $P > 0.9$.

## Fore-Arm Flow Rates

### Control Group; Reproducibility Between Intervals

| | Interval | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| | 3.9 | 5.9 | 9.0 | 4.0 | 4.2 | 9.1 |
| | 2.5 | 1.8 | 1.4 | 2.1 | 1.6 | 1.5 |
| | 5.4 | 4.2 | 4.6 | 4.7 | 3.8 | 2.4 |
| | 2.6 | 3.1 | 2.7 | 3.1 | 2.9 | 1.3 |
| | 1.2 | 1.6 | 1.2 | 1.6 | 2.6 | 6.3 |
| | 2.2 | 3.2 | 6.4 | 2.6 | 5.3 | 3.9 |
| | 4.5 | 2.4 | 3.4 | 3.2 | 4.0 | 6.0 |
| | 5.2 | 5.6 | 7.5 | 7.0 | 7.5 | 4.1 |
| | 4.0 | 3.7 | 4.1 | 3.0 | 1.7 | 2.5 |
| | 7.1 | 5.2 | 8.0 | 5.7 | 2.6 | 2.5 |
| | 2.0 | 0.8 | 2.5 | 2.3 | 4.5 | 5.4 |
| | 2.8 | 4.3 | 3.3 | 2.4 | 2.3 | 5.0 |
| | 2.1 | 3.6 | 1.6 | 2.1 | 2.6 | 1.6 |
| | 5.4 | 5.4 | 3.2 | 3.6 | 3.7 | 3.4 |
| Mean | 3.64 | 3.63 | 4.21 | 3.84 | 3.52 | 3.93 |
| S.D. | 1.70 | 1.59 | 2.55 | 1.64 | 1.57 | 2.23 |

Table 2

9. The Effect of Fore-Arm Skin Temperature and Fore-Arm Blood Flow (Figure 11)

Fore-arm skin temperature rose significantly with fore-arm blood flow. The calculation of the regression curve of flow on skin temperature gave b = 0.669, t = 3.396 on 57 degrees of freedom, $0.01 > P > 0.001$.

10. The Relationship of the Temperature Gradient between Body and Fore-Arm Skin Temperature and Fore-Arm Blood Flow (Figure 12)

The temperature gradient between body and fore-arm skin decreased significantly as the fore-arm flow rate rose. The calculation of a regression curve gave b = -0.746, t = 3.599 on 57 degrees of freedom, $P < 0.001$.

11. ,Pulse Rate and Fore-Arm Flow

No relationship could be demonstrated between pulse rate and fore-arm flow rates; t = 1.607 on 97 degrees of freedom, $0.2 > P > 0.1$.

12. Pulse Pressure and Fore-Arm Flow

No relationship could be demonstrated between pulse pressure and fore-arm blood flow rates; t = 0.568 on 113 degrees of freedom, $0.6 > P > 0.5$.

13. Blood Pressure and Fore-Arm Flow

Of the thirty-two non-pregnant control subjects twenty-two subjects were included in the normotensive range, as defined earlier, and ten subjects were included in the hypertensive group. The mean blood pressures were 113/68 mm. Hg. and 128/80 mm. Hg. respectively. Comparing the systolic pressures and diastolic pressures showed significant differences; t = 5.333 on 30 degrees of freedom, $P < 0.001$ for systolic pressure and t = 5.356 on 30 degrees of freedom, $P < 0.001$ for diastolic pressure.

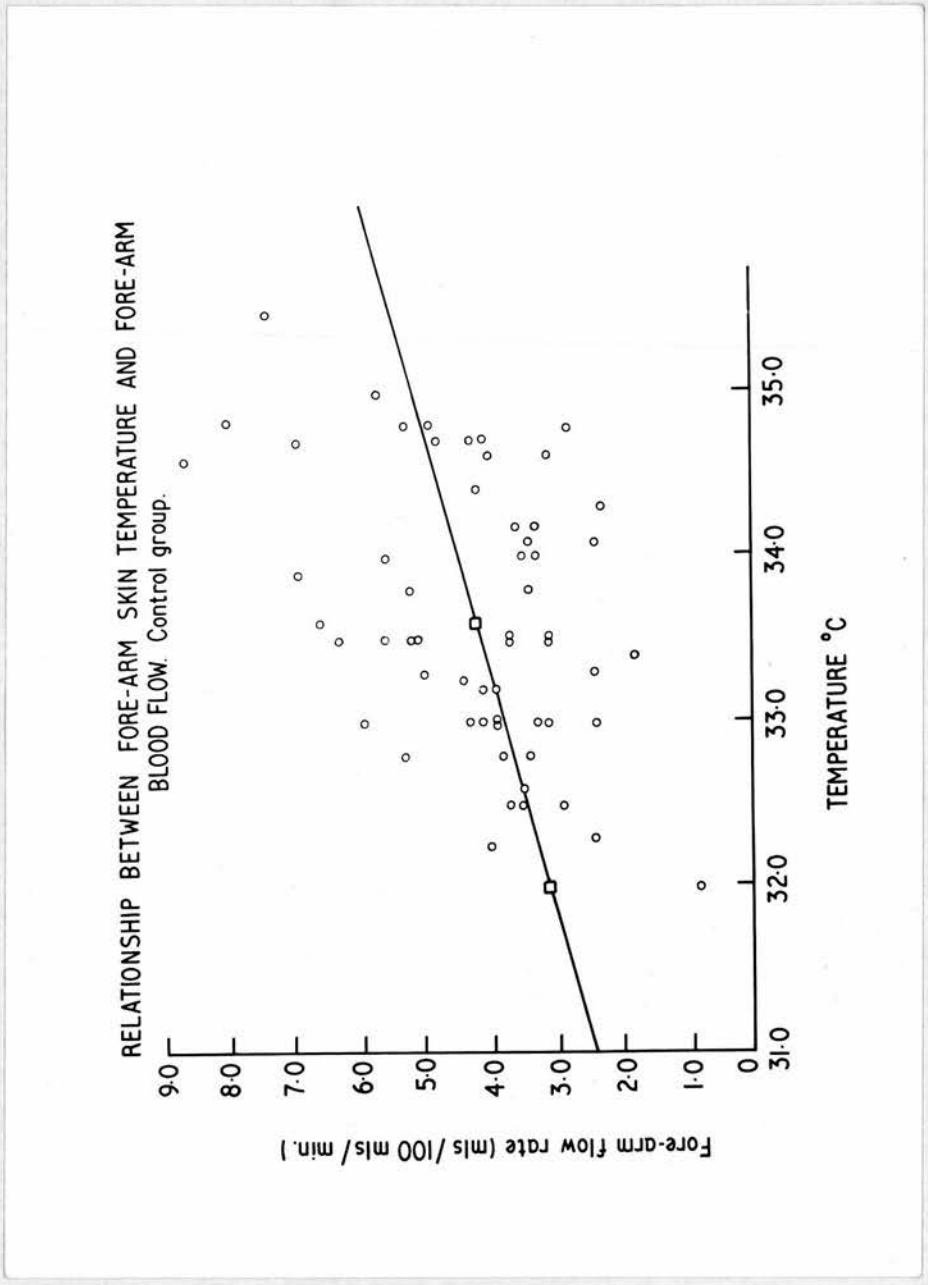



Figure XI

Relationship between fore-arm skin temperature and fore-arm blood flow rates in the control group. The regression line of flow on temperature is represented by the open squares and continuous line.

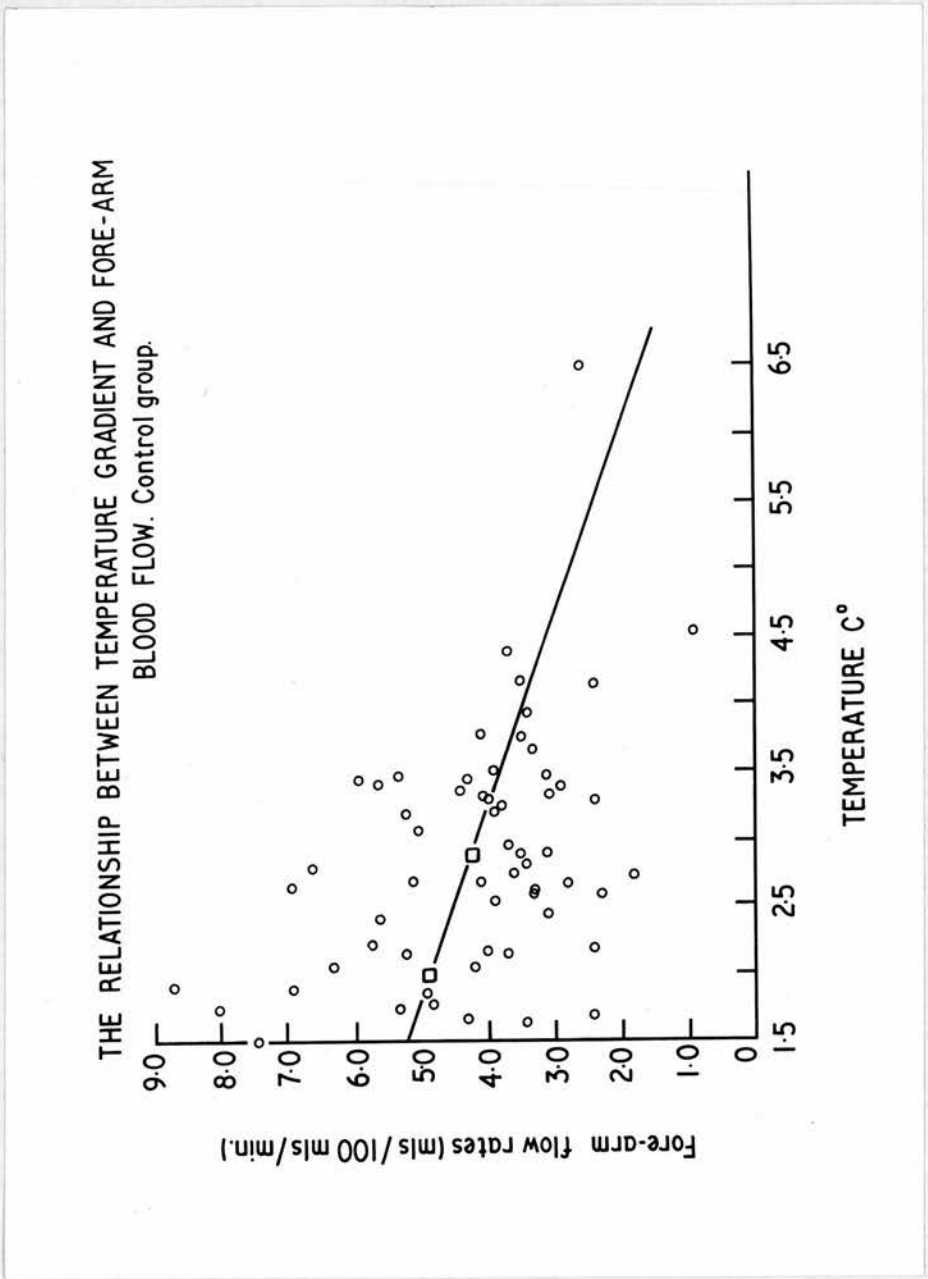



Figure XII

Relationship between temperature gradient between oral and fore-arm temperatures and fore-arm blood flow rates in the control group. The regression line of flow on temperature is represented by the open squares and continuous line.

The average fore-arm flow rate for the normotensive group was 3.9 mls./100 mls./minute ± S.D. 1.62, and that for the hypertensive group was 4.0 mls./100 mls./minute ± S.D. 1.89.

(a) The systolic pressure

No relationship could be demonstrated between systolic blood pressure and fore-arm flow; $t = 1.143$ on 113 degrees of freedom, $0.3 > P > 0.2$.

(b) The diastolic pressure

No relationship could be demonstrated between diastolic blood pressure and fore-arm flow; $t = 0.109$ on 113 degrees of freedom, $P > 0.9$.

14. Blood Volume and Fore-Arm Flow

No relationship could be demonstrated between the mean blood volume for the period 6 weeks to 40 weeks after delivery and the mean flow rate for the same period; $t = -1.672$ on 64 degrees of freedom, $0.1 > P > 0.05$.

15. The Haemoglobin Level and Fore-Arm Flow

No relationship could be demonstrated between the mean haemoglobin level and mean fore-arm flow; $t = -0.554$ on 108 degrees of freedom, $0.6 > P > 0.5$.

## Summary

1. There was a significant reduction in fore-arm flow rate with increasing age.
2. There was a significant increase in fore-arm skin temperature with increasing fore-arm flow rate.
3. There was a significant decrease in difference between body and fore-arm skin temperature with increased fore-arm flow.
4. No significant relationship could be demonstrated between fore-arm flow rates and the following parameters:

   (i) parity
   (ii) body surface area
   (iii) smoking habits
   (iv) stage of menstrual cycle
   (v) season
   (vi) normal body temperature
   (vii) pulse rate
   (viii) pulse pressure
   (ix) blood pressure
   (x) blood volume
   (xi) haemoglobin level.

5. Over a seven month period fore-arm flow rates were reproducible within subjects.

## FORE-ARM BLOOD FLOW RATES IN PREGNANCY

### The Experimental Groups

#### I - The Normotensive Group

Subjects:

Twenty-six subjects were examined on between nine and thirteen occasions each; a total of 295 readings were obtained. The mean age was 23.3 years ± S.D. 3.5 and the range was 18 to 35 years. Eighteen of the subjects were primigravidæ and the remainder had between 1 and 5 children each. The mean height was 63.8 inches ± S.D. 2.3 and the mean weight at first visit was 123.3 lbs. ± S.D. 14.9. The mean surface area at first visit was 1.58 square metres ± S.D. 0.11. The mean birth weight was 3288 grammes ± S.D. 495.6.

Results:

The mean fore-arm flow rate with the standard deviation and standard error of the mean for each stage of gestation and period after delivery with t-values, degrees of freedom and P values for comparison with the non pregnant group are enumerated in the Table 3 . The corrected readings were obtained by calculating the mean change in flow rate shown by those subjects who were examined in both the interval for correction and the previous interval. The mean change was added to the mean flow rate for the previous interval to obtain a figure for the corrected interval which would reflect the real change between these two intervals.

Table 3

The Normotensive Group

| Weeks Gestation | Number of Subjects | Mean Flow in mls./100 mls. per minute. | S.D. | S.E. | Non-Pregnant Mean Flow | Number of Subjects | t | Degrees of freedom | P |
|---|---|---|---|---|---|---|---|---|---|
| 8 | 22 | 2.6 | 1.05 | 0.22 | 4.0 | 32 | 3.454 | 52 | 0.01-0.001 |
| 12 | 26 | 3.2 | 1.89 | 0.37 | | | | | |
| 16 | 25 | 2.7 | 1.59 | 0.32 | | | | | |
| 20 | 25 | 2.8 | 1.26 | 0.25 | | | | | |
| 24 | 26 | 3.3 | 2.02 | 0.40 | | | 1.443 | 56 | 0.2 -0.1 |
| 28 | 26 | 3.4 | 2.51 | 0.49 | | | | | |
| 32 | 26 | 3.5 | 1.83 | 0.36 | | | | | |
| 36 | 21 | 3.2 | 1.91 | 0.42 | | | 1.610 | 51 | 0.2 -0.1 |
| 40 + over | 9 | 3.9 | 1.68 | 0.56 | | | not | different | |
| (corrected) | | 3.9 | | | | | | | |
| Post-Delivery | | | | | | | | | |
| 3rd day | 24 | 4.6 | 2.67 | 0.55 | | | 1.030 | 54 | 0.4 -0.3 |
| 6 weeks | 26 | 3.1 | 1.32 | 0.26 | | | 2.230 | 56 | 0.05-0.02 |
| 12 weeks | 24 | 4.7 | 2.63 | 0.54 | | | | | |
| 40 weeks | 15 | 4.1 | 2.06 | 0.53 | | | not | different | |
| (corrected) | | 4.4 | | | | | | | |

There is a significant increase in fore-arm blood flow from 8 - 11 weeks gestation to 32 - 35 weeks gestation. A paired t-test on the differences between the flows for each subject present in the 32 - 35 week interval and the first visit interval gave a mean increase of flow of 1.0 mls./100 mls./minute $\pm$ S.D. 2.2; $t = 2.310$ on 25 degrees of freedom, $0.05 > P > 0.02$.

The period of gestation at which a subject attains her maximum flow rate varies. In order to obtain a true picture of the degree of change for each subject the maximum change from 8 - 11 weeks gestation was calculated regardless of the period during which this change took place. The mean maximum change in flow rate throughout pregnancy was +2.9 mls./100 mls./minute $\pm$ S.D. 2.5 and had occurred, on average, at 24 - 27 weeks gestation. A paired t-test gave $t = 5.857$ on 25 degrees of freedom, $P < 0.001$.

After delivery a further increase in mean flow rate occurred. A paired t-test on the mean change in flow from first visit to third day after delivery showed a mean increase of 2.2 mls./100 mls. per minute $\pm$ S.D. 2.6; $t = 4.165$ on 23 degrees of freedom, $P < 0.001$.

By six weeks after delivery the flow rate had dropped from the third day figure by a mean of 1.5 mls./100 mls./minute $\pm$ S.D. 2.5; $t = 2.97$ on 23 degrees of freedom, $0.01 > P > 0.001$, but was still significantly higher than the first visit flow rate by a mean of 0.6 mls./100 mls./minute $\pm$ S.D. 2.6; $t = 2.33$ on 25 degrees of freedom, $0.05 > P > 0.02$. The six patients who were still breast-feeding at 6 weeks after delivery showed a larger drop in flow from the third day than those who were artificially feeding. The mean fall for the subjects breast-feeding was 3.5 mls./100 mls./minute $\pm$ S.D. 3.7 and

that for patients artificially feeding was 0.8 mls./100 mls. per minute ± S.D. 1.53; t = 2.528 on 22 degrees of freedom, $0.02 > P > 0.01$. This was the only group in which this difference was shown.

At twelve weeks after delivery the mean flow rate was still 2.3 mls./100 mls./minute ± S.D. 2.8 faster than the flow at first visit. A paired t-test gave t = 3.94 on 23 degrees of freedom, $P < 0.001$.

Fifteen patients were examined nine months after delivery. The mean increase in flow rate over the first visit reading was 1.7 mls./100 mls./minute ± S.D. 2.5. A paired t-test gave t = 2.636 on 14 degrees of freedom, $0.02 > P > 0.01$.

Reproducibility between the first two visits:

From 8 - 11 weeks gestation to 12 - 15 weeks gestation there was a mean increase in flow rate of 1.0 mls./100 mls./minute ± S.D. 3.3. A paired t-test gave t = 2.539 on 21 degrees of freedom, $0.02 > P > 0.01$.

The fore-arm blood flow rate of the normotensive group compared with the non-pregnant control group:

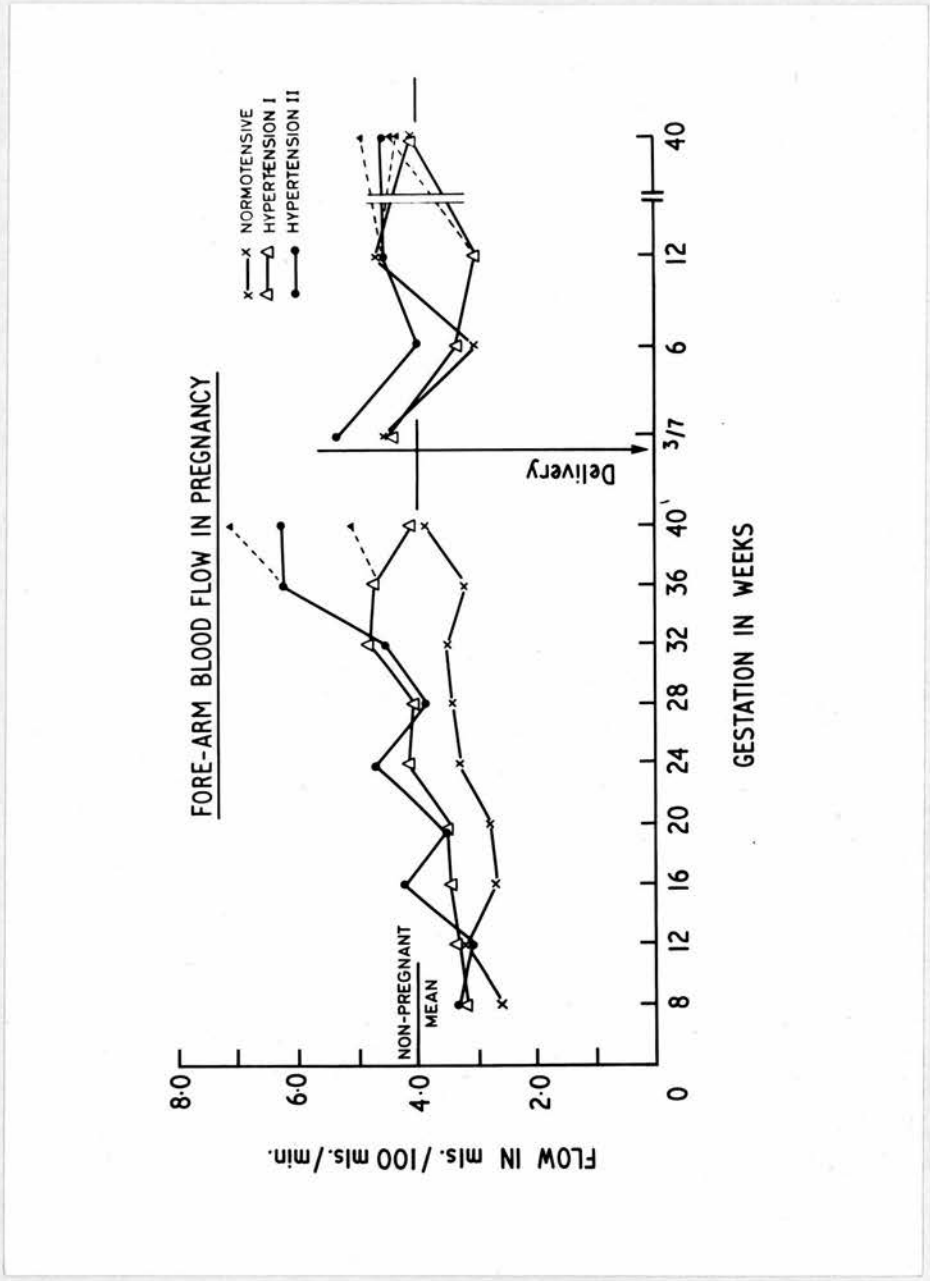
At the first visit the flow rate in the normotensive pregnant group was 2.6 mls./100 mls./minute ± S.D. 1.1 and was significantly lower than that of the non-pregnant control group which was 4.0 mls. per 100 mls./minute ± S.D. 1.7; t = 3.454 on 52 degrees of freedom, $0.01 > P > 0.001$.

As pregnancy advanced the flow-rate of the normotensive group approached the non-pregnant level and at 24-27 weeks gestation was not significantly different from the non-pregnant group; t = 1.443 on 51 degrees of freedom, $0.2 > P > 0.1$. The flow rate for the pregnant group never exceeded the mean non-pregnant level.

On the third day after delivery the mean flow rate exceeded that of the non-pregnant group for the first time but not significantly; $t = 1.030$ on 54 degrees of freedom, $0.4 > P > 0.3$.

At six weeks after delivery the mean flow rate was 3.1 mls. per 100 mls./minute $\pm$ S.D. 1.32 which was just significantly lower than the non-pregnant level; $t = 2.230$ on 56 degrees of freedom, $0.05 > P > 0.02$. This effect was due to those patients who were still breast-feeding.

Nine months after delivery the normotensive group mean flow rate closely approximated the non-pregnant level.




## Table XIII

Fore-arm blood flow in pregnancy. The continuous lines join the means for all the patients in each blood pressure group. The means are represented by symbols explained in the key in the diagram. The broken lines and closed triangles represent the corrected readings.

N.B.
For clarity in this Figure and subsequent Figures the ante-natal intervals are represented by the earliest week of each interval, e.g. 8 weeks is equivalent to the interval 8 - 11 weeks gestation.

II - The Hypertensive Group I

Subjects:

Twenty four subjects were examined on between 7 and 13 occasions each; a total of 259 readings were obtained. The mean age was 23.2 years ± S.D. 4.1, range 18 to 35 years. Eighteen of the subjects were primigravidae and the remainder had between 1 and 2 children each. The mean height was 63.8 inches ± S.D. 2.3 and the mean weight at first visit was 125.8 lbs. ± S.D. 14.3. The mean surface area at first visit was 1.59 square metres ± S.D. 0.10. The mean birthweight was 3243 grammes ± S.D. 337.6.

Results:

The mean fore-arm flow rate with the standard deviation, and standard error of the mean for each stage of gestation and period after delivery, with t values, degrees of freedom and P values for comparisons with the non-pregnant group are shown in Table (4).

There was a significant increase in fore-arm blood flow from 8 - 11 weeks gestation to 36 - 39 weeks gestation of 1.5 mls. per 100 mls./minute ± S.D. 3.1. A paired t-test on the differences between the first visit and 36 - 39 week flow rates gave $t = 2.360$ on 23 degrees of freedom, $0.05 > P > 0.02$; but, up to 32 - 35 weeks gestation the mean increasewas not significant; $t = 1.999$ on 23 degrees of freedom, $0.1 > P > 0.05$.

The mean maximum change in flow rate throughout pregnancy was +4.6 mls./100 mls./minute ± S.D. 3.1 and had occurred, on average, at 28 - 31 weeks. A paired t-test gave $t = 7.258$ on 23 degrees of freedom, $P < 0.001$.

Table 4

The Hypertension I Group

| Weeks Gestation | Number of Subjects | Mean Flow in mls./100 mls. per minute. | S.D. | S.E. | Non-Pregnant Mean Flow | Number of Subjects | t | Degrees of freedom | P |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | (all hypert.) | |
| 8 | 21 | 3.2 | 1.63 | 0.36 | 4.0 | 32 | 2.016 | 81 | 0.05-0.02 |
| 12 | 21 | 3.3 | 1.92 | 0.42 | | | | | |
| 16 | 24 | 3.4 | 1.83 | 0.37 | | | | | |
| 20 | 22 | 3.5 | 2.11 | 0.45 | | | | | |
| 24 | 23 | 4.1 | 2.38 | 0.50 | | | not | different | |
| 28 | 22 | 4.0 | 2.37 | 0.51 | | | not | different | |
| 32 | 23 | 4.8 | 4.41 | 0.92 | | | 0.938 | 53 | 0.4 -0.3 |
| 36 | 24 | 4.7 | 2.82 | 0.58 | | | 1.160 | 54 | 0.3 -0.2 |
| 40 + over | 4 | 4.1 | 2.22 | 1.11 | | | | | |
| (corrected) | | 5.1 | | | | | | | |
| Post-Delivery | | | | | | | | | |
| 3rd day | 24 | 4.6 | 2.28 | 0.47 | | | 1.135 | 54 | 0.3 -0.2 |
| 6 weeks | 23 | 3.3 | 1.74 | 0.36 | | | 1.500 | 53 | 0.2 -0.1 |
| 12 weeks | 18 | 3.0 | 1.52 | 0.36 | | | 2.089 | 48 | 0.05-0.02 |
| 40 weeks | 10 | 4.1 | 1.13 | 0.36 | | | not | different | |
| (corrected) | | 4.5 | | | | | | | |

The mean flow rate on the 3rd day after delivery did not differ from the flows occuring from 32 weeks gestation to delivery, and differed from the first visit flow by + 1.4 mls./100 mls./minute ± S.D. 2.1; t = 3.230 on 23 degrees of freedom, $0.01 > P > 0.001$.

By six weeks after delivery there was a mean fall in the flow rate of 1.4 mls./100 mls./minute ± S.D. 2.5 from the third day level; t = 2.765 on 22 degrees of freedom, $0.02 > P > 0.01$, and this level did not differ significantly from the readings obtained in the first four intervals during pregnancy. The 10 patients who were breast-feeding showed a fall of 1.5 mls./100 mls./minute, and those who were feeding artificially showed a fall of 1.4 mls./100 mls./minute. Unlike the effect in the normotensive group there was no difference due to the type of feeding.

At twelve weeks after delivery the flow rate did not differ from that of the first visit; t = 0.551 on 17 degrees of freedom, $0.6 > P > 0.5$.

Ten patients were examined at 9 months after delivery. There was a mean increase of 1.0 mls./100 mls./minute ± S.D. 1.6 over the first visit flow which was not significant on a paired t-test; t = 1.864 on 9 degrees of freedom, $0.1 > P > 0.05$.

Reproducibility between the first two visits:

A paired t-test on the difference between flows at 8 - 11 weeks and 12 - 15 weeks gestation showed a mean difference of -0.2mls. per 100 mls./minute ± S.D. 2.0 which was not significant; t = 0.505 on 18 degrees of freedom, $0.7 > P > 0.6$.

The fore-arm blood flow rate of the Hypertension I Group compared with the non-pregnant control group:

At the first visit, 8 - 11 weeks gestation, the flow rate was

significantly lower than that of the non-pregnant group; $t = 2.016$ on 81 degrees of freedom, $0.05 > P > 0.02$. (For convenience, all hypertensive patients have been included in this t-test against the non-pregnant group as there was no difference between the means of the hypertensive groups at this interval.)

As pregnancy advanced the mean flow rate approached that of the non-pregnant group and by 24 - 27 weeks gestation the flow rates were the same. By 36 - 39 weeks gestation the mean flow rate in the pregnant group was higher than that of the non-pregnant group but not significantly so; $t = 1.160$ on 54 degrees of freedom, $0.3 > P > 0.2$.

At three days and six weeks following delivery the mean flow rates did not significantly differ from the non-pregnant group; $t = 1.135$ on 54 degrees of freedom, $0.3 > P > 0.2$ and $t = 1.150$ on 53 degrees of freedom, $0.2 > P > 0.1$ respectively.

At twelve weeks after delivery the flow rates were significantly lower than the non-pregnant group by a mean of 1.0 mls./100 mls. per minute; $t = 2.0887$ on 48 degrees of freedom, $0.05 > P > 0.02$ but by nine months after delivery the flow rates were the same as the non-pregnant group.

III - The Hypertensive Group II

Subjects:

Thirty-six subjects were examined on between six and thirteen occasions each; a total of 393 readings were obtained. The mean age was 22.9 years ± S.D. 3.7; range 17 years to 32 years. Twenty-nine of the patients were primigravidæ and the remainder had between one and two children each. The mean height was 64.4 inches ± S.D. 2.4 and the mean weight at first visit was 126.2 lbs. ± S.D. 12.41. The mean surface area at first visit was 1.62 square metres ± S.D. 0.11. The mean birthweight was 3367 grammes ± S.D. 458.8.

Results:

The mean fore-arm flow rate with the standard deviation and standard error of the mean for each stage of gestation and period after delivery, with t-values, degrees of freedom and P-values for comparison with the non-pregnant group are shown in Table (5).

There was a significant increase in the fore-arm blood flow rate from 8 - 11 weeks gestation to 32 - 35 weeks gestation. A paired t-test showed a mean increase of 1.2 mls./100 mls./minute ± S.D. 3.2; $t = 2.325$ on 35 degrees of freedom, $0.05 > P > 0.02$. From 8 - 11 weeks to 36 - 39 weeks gestation the mean increase was 2.7 mls./100 mls./minute ± S.D. 5.9; $t = 2.708$ on 33 degrees of freedom, $0.02 > P > 0.01$. The mean maximum change in flow rate throughout pregnancy was +5.2 mls./100 mls./minute ± S.D. 5.7; $t = 5.488$ on 35 degrees of freedom, $P < 0.001$. The maximum change occurred on average by 28 to 31 weeks gestation.

Table 5

The Hypertension II Group

| Weeks Gestation | Number of Subjects | Mean Flow in mls./100 mls. per minute. | S.D. | S.E. | Non-Pregnant Mean Flow | Number of Subjects | t | Degrees of Freedom | P |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | (All hyper.) | |
| 8 | 30 | 3.3 | 1.54 | 0.28 | 4.0 | 32 | 2.016 | 81 | 0.05-0.02 |
| 12 | 32 | 3.1 | 1.40 | 0.25 | | | | | |
| 16 | 34 | 4.2 | 2.39 | 0.41 | | | not | different | |
| 20 | 35 | 3.5 | 1.71 | 0.29 | | | | | |
| 24 | 34 | 4.7 | 3.24 | 0.56 | | | | | |
| 28 | 35 | 3.9 | 2.29 | 0.39 | | | | | |
| 32 | 35 | 4.6 | 2.71 | 0.46 | | | | | |
| 36 | 34 | 6.2 | 5.21 | 0.89 | | | 2.280 | 64 | 0.05-0.02 |
| 40 + over | 15 | 6.2 | 4.34 | 1.12 | | | | | |
| (corrected) | | 7.2 | | | | | | | |
| Post-Delivery | | | | | | | | | |
| 3rd day | 35 | 5.3 | 2.46 | 0.42 | | | 2.502 | 65 | 0.02-0.01 |
| 6 weeks | 33 | 4.0 | 1.83 | 0.32 | | | not | different | |
| 12 weeks | 27 | 4.6 | 2.88 | 0.55 | | | | | |
| 40 weeks | 14 | 4.6 | 2.97 | 0.79 | | | 0.873 | 44 | 0.4 -0.3 |
| (corrected) | | 5.0 | | | | | | | |

Following delivery there was a fall in flow rate to a level which was on average 1.8 mls./100mls./minute ± S.D. 3.8 greater than the first visit flow; t = 3.800 on 31 degrees of freedom, $P < 0.001$.

By six weeks after delivery there had been a further significant fall from the third day level of 1.3 mls./100 mls. ± S.D. 2.6 per minute on average; t = 2.598 on 32 degrees of freedom, $0.02 > P > 0.01$, and this new level was not significantly higher than that for the first visit; t = 1.208 on 32 degrees of freedom, $0.3 > P > 0.2$. As in the Hypertension I Group the type of feeding did not change the degree of fall from the third day reading. In patients who breast-fed the mean fall was 1.4 mls./100 mls./minute ± S.D. 5.2 and in patients who were not breast-feeding the mean fall was 1.2 mls. per 100 mls./minute ± S.D. 8.8.

At twelve weeks after delivery the flow rate had increased by a mean of 1.3 mls./100 mls./minute ± S.D. 2.6 over the first visit reading; t = 2.550 on 25 degrees of freedom, $0.02 > P > 0.01$, and at nine months after delivery the mean increase over the first reading had remained the same, i.e. 1.4 mls./100 mls./minute ± S.D. 2.7.

Reproducibility in the first two readings in pregnancy:

The mean difference between readings taken at 12 - 15 weeks gestation and 8 - 11 weeks gestation was -0.3 mls./100 mls./minute ± S.D. 1.7; t = 1.083 on 29 degrees of freedom, $0.3 > P > 0.2$.

The fore-arm blood flow rate of the Hypertension II Group compared with the non-pregnant group:

The mean fore-arm flow rate at 8 - 11 weeks gestation was significantly lower than the non-pregnant mean flow rate; t = 2.016 on 81 degrees of freedom, $0.05 > P > 0.02$ (see Hypertension I Group, page 70 ).

During pregnancy there was a mean increase in flow and at 36 - 39 weeks gestation the flow rate was 2.2 mls./100 mls./minute greater than the non-pregnant mean; $t = 2.280$ on 64 degrees of freedom, $0.05 > P > 0.02$.

On the third day after delivery the mean flow rate had fallen but was still greater than the non-pregnant rate by 1.3 mls./100 mls. per minute; $t = 2.502$ on 65 degrees of freedom, $0.02 > P > 0.01$.

Six weeks after delivery the mean flow rates were the same. Following this there was a slight but insignificant increase over the non-pregnant rate of 0.6 mls./100 mls./minute; $t = 0.873$ on 44 degrees of freedom, $0.4 > P > 0.3$ at nine months post-delivery.

## Comparison of the Experimental Groups

1. Age

Although a slight decrease in fore-arm blood flow rate had been shown to occur with increasing age, the mean ages of the three experimental groups were not significantly different and would not affect comparison between the groups.

2. Parity

Parity had no effect on fore-arm blood flow rate in the non-pregnant state. There was no difference in incidence of primigravidae and multigravidae in the experimental groups; $\chi^2 = 1.05$ on 2 degrees of freedom, $0.7 > P > 0.5$.

3. Surface Area

Body surface area had no effect on fore-arm blood flow rates in the non-pregnant state. There was no significant difference in the mean body surface areas of the experimental groups; e.g. comparing the normotensive group with the hypertension II group gave $t = 1.437$ on 60 degrees of freedom, $0.2 > P > 0.1$.

4. Smoking

There was no significant difference between the mean flow rates of the control group comparing non-smokers with smokers. Similarly there was no significant difference between the flow rates of the experimental groups at first visit compared with smoking habits; $F = 0.14$ on $1/2$ degrees of freedom, and no significant difference in the changes in flow rate during pregnancy compared with smoking habits; $F = 0.068$ on $1/2$ degrees of freedom.

5. Reproducibility between the First Two Intervals

There was no significant decrease in fore-arm flow rates from the first to second intervals in any of the experimental groups indicating that there was no significant stress factor operating in the first interval.

6. Seasonal Effect

Changes in blood flow rate could not be ascribed to a seasonal effect. (See Page 55.)

7. Haemoglobin Level

There was no significant difference between haemoglobin levels at the first visit. Details are given in section from page 167.

8. Blood Volume

There was no significant difference between blood volume levels at first visit for each experimental group. Changes occurring thereafter are described in section from page 159.

9. Gain in weight during pregnancy

No significant differences were found between blood pressure groups.

10. Birth Weight

There was no significant difference between mean birth weights for each blood pressure group, e.g. comparing the two hypertensive groups, $t = 1.174$ on 58 degrees of freedom, $0.3 > P > 0.2$.

SUMMARY

Differences in fore-arm blood flow rates between the experimental groups could not be ascribed to age, parity, height, weight, surface area, season, stress or smoking habits. The groups did not differ in haemoglobin level and blood volume at first visit. The effect of other factors are described from page 83 to page 89.

| | | Non-pregnant | Normotensive | Hypertension I | Hypertension II | Others | Total |
|---|---|---|---|---|---|---|---|
| Number of Subjects | | 32 | 26 | 24 | 36 | 9 | 127 |
| Number of Readings | | 152 | 295 | 259 | 393 | 50 | 1,149 |
| Age (Years) | Mean | 26.5 | 23.3 | 23.2 | 22.9 | | |
| | S.D. | 4.5 | 3.5 | 4.1 | 3.7 | | |
| | Range | 19-35 | 18-35 | 18-35 | 17-32 | | |
| Parity | 0 | 31 | 18 | 18 | 29 | | |
| | 1 | 0 | 6 | 4 | 5 | | |
| | 2 & over | 1 | 2 | 2 | 2 | | |
| Height (inches) | Mean | 65.2 | 63.8 | 63.8 | 64.4 | | |
| | S.D. | 2.3 | 2.3 | 2.3 | 2.4 | | |
| Weight (lbs.) | Mean | 134.8 | 123.3 | 125.8 | 126.8 | | |
| | S.D. | 16.09 | 14.9 | 14.3 | 12.4 | | |
| Surface Area (sq. metres) | Mean | 1.67 | 1.58 | 1.59 | 1.62 | | |
| | S.D. | 0.11 | 0.11 | 0.10 | 0.11 | | |
| Weight gain (lbs.) | Mean | 2.44 | 22.1 | 22.5 | 22.4 | | |
| | S.D. | 2.80 | 8.2 | 5.8 | 7.1 | | |
| Birth Weight (grammes) | Mean | - | 3288 | 3243 | 3367 | | |
| | S.D. | - | 495.6 | 337.6 | 458.8 | | |

Table 6

## The Relationship Between the Three Experimental Groups

### Ante-natal changes in fore-arm blood flow

From the first visit to 32 - 35 weeks gestation there was no significant difference in the changes in flow. Comparing the change in normotensive flow rate with that of the combined hypertensive groups over this period gave $t = 0.488$ on 84 degrees of freedom, $0.7 > P > 0.6$.

Comparing the maximum increases in flow rate during pregnancy the hypertension I group increased by 1.7 mls./100 mls./minute more than the normotensive group; $t = 2.182$ on 48 degrees of freedom, $0.05 > P > 0.02$, and the hypertension II group increased by 0.6 mls.per 100 mls./minute more than the hypertension I group; $t = 0.493$ on 58 degrees of freedom, $0.7 > P > 0.6$.

At 8 - 11 weeks gestation the hypertensive groups had a mean flow rate slightly higher than the normotensive group but not significantly so; $t = 1.564$ on 71 degrees of freedom, $0.2 > P > 0.1$; and at 12 - 15 weeks gestation all three groups had very similar flow rates.

At 32 - 35 weeks gestation the difference between the normotensive group and the hypertensive groups had increased but the difference was not significant; $t = 1.784$ on 59 degrees of freedom, $0.1 > P > 0.5$.

At 36 - 39 weeks gestation the hypertensive groups had significantly risen above the normotensive flow rates; $t = 2.406$ on 77 degrees of freedom, $0.02 > P > 0.01$, but the hypertensive groups did not differ significantly from each other; $t = 1.283$ on 56 degrees of freedom, $0.3 > P > 0.2$. Although the mean difference in flow rate between the hypertensive groups at 36 - 39 weeks gestation was 1.5mls.

per 100 mls/minute the ranges were wide.

On the third day after delivery the mean flow rate of the normotensive group was the same as that of the hypertension I group and although lower than that of the hypertension II group did not significantly differ from it; $t = 1.036$ on 57 degrees of freedom, $0.4 > P > 0.3$.

Six weeks after delivery the normotensive flow rate again approximated that of the hypertension I group but was significantly lower than the hypertension II group; $t = 2.107$ on 57 degrees of freedom, $0.05 > P > 0.02$.

At twelve weeks after delivery the normotensive group flow rate was the same as that for the hypertension II group and was significantly higher than the hypertension I group; $t = 2.448$ on 40 degrees of freedom, $0,02 > P > 0.01$.

By nine months after delivery the flow rates for all groups were not significantly different from each other.

## Summary of Changes in Fore-arm Blood Flow Rate During Pregnancy and up to Nine Months after Delivery

1. The mean fore-arm flow rates in early pregnancy were significantly lower than the non-pregnant mean flow rate and the mean flow rates at 40 weeks after delivery. There was no significant difference between the blood pressure groups at these times.

2. There was a significant increase in the mean fore-arm blood flow rate with advancing pregnancy in all blood pressure groups. The normotensive group showed the smallest increase and the hypertension II group showed the greatest increase.

The normotensive group mean flow rate remained significantly below the non-pregnant level until 24 - 27 weeks gestation and thereafter remained close to the non-pregnant level but never equalled it.

The hypertensive groups reached non-pregnant levels by 16 - 19 weeks gestation and continued to rise but the hypertension I group never became significantly higher than the non-pregnant level. The hypertension II group became significantly higher than the non-pregnant level at 36 - 39 weeks gestation. Both hypertensive groups attained significantly higher flow rates than the normotensive group at 36 weeks gestation.

3. On the third post-natal day the hypertensive groups showed a decrease in flow rate compared with the pre-delivery figure but only the hypertension II group remained significantly higher than the non-pregnant level. The flow rate of the normotensive group was higher than at any time before delivery, having exceeded the non-pregnant level but was not significantly higher than the non-pregnant level.

All groups showed a drop in flow at six weeks after delivery. By twelve weeks after delivery the normotensive and hypertension II groups had risen to attain their "non-pregnant" level but the hypertension I group remained significantly lower and attained non-pregnant levels forty weeks after delivery.

4. At forty weeks after delivery the experimental groups mean flow rates were very similar and did not significantly differ from the non-pregnant control group mean.

## The Relationship Between Fore-Arm Blood Flow Rates and Other Physiological Measurements

### 1. The Relationship between change in Fore-Arm Blood Flows and Change in Blood Pressure

#### (a) Systolic pressure

There was no relationship between the maximum change in fore-arm blood flow and the change in systolic pressure recorded during pregnancy; $t = 0.133$ on 83 degrees of freedom, $0.9 > P > 0.8$.

#### (b) Diastolic pressure

There was a significant relationship between the maximum increase in fore-arm blood flow rate and change in diastolic level during pregnancy. A regression analysis gave $b = 0.173$; $t = 5.584$ on 83 degrees of freedom, $P < 0.001$. An increase of 5 mm. Hg. in diastolic gave a mean increase in flow rate of 2.8 mls./100 mls. per minute and an increase in diastolic of 14 mm. Hg. gave a mean increase in flow rate of 4.4 mls./100 mls./minute. See Figure(XIV).

### 2. Fore-Arm Blood Flow and Pulse Rate

There was no relationship between maximum change in fore-arm flow rate and maximum change in pulse rate. For normotensive group $t = 0.364$ on 19 degrees of freedom, $0.8 > P > 0.7$, for the hypertension I group $t = 0.477$ on 21 degrees of freedom, $0.7 > P > 0.6$ and for the hypertension II group $t = -1.594$ on 27 degrees of freedom, $0.2 > P > 0.1$.

### 3. Fore-Arm Blood Flow Rate and Blood Volume

There was no relationship between maximum increase in fore-arm flow rate and maximum increase in blood volume; $t = 0.894$ on 65 degrees of freedom, $0.4 > P > 0.3$.

### 4. Change in Fore-Arm Flow Rate and Change in Temperature Gradient (Body temperature minus skin temperature)

There was no significant relationship between change in flow rate

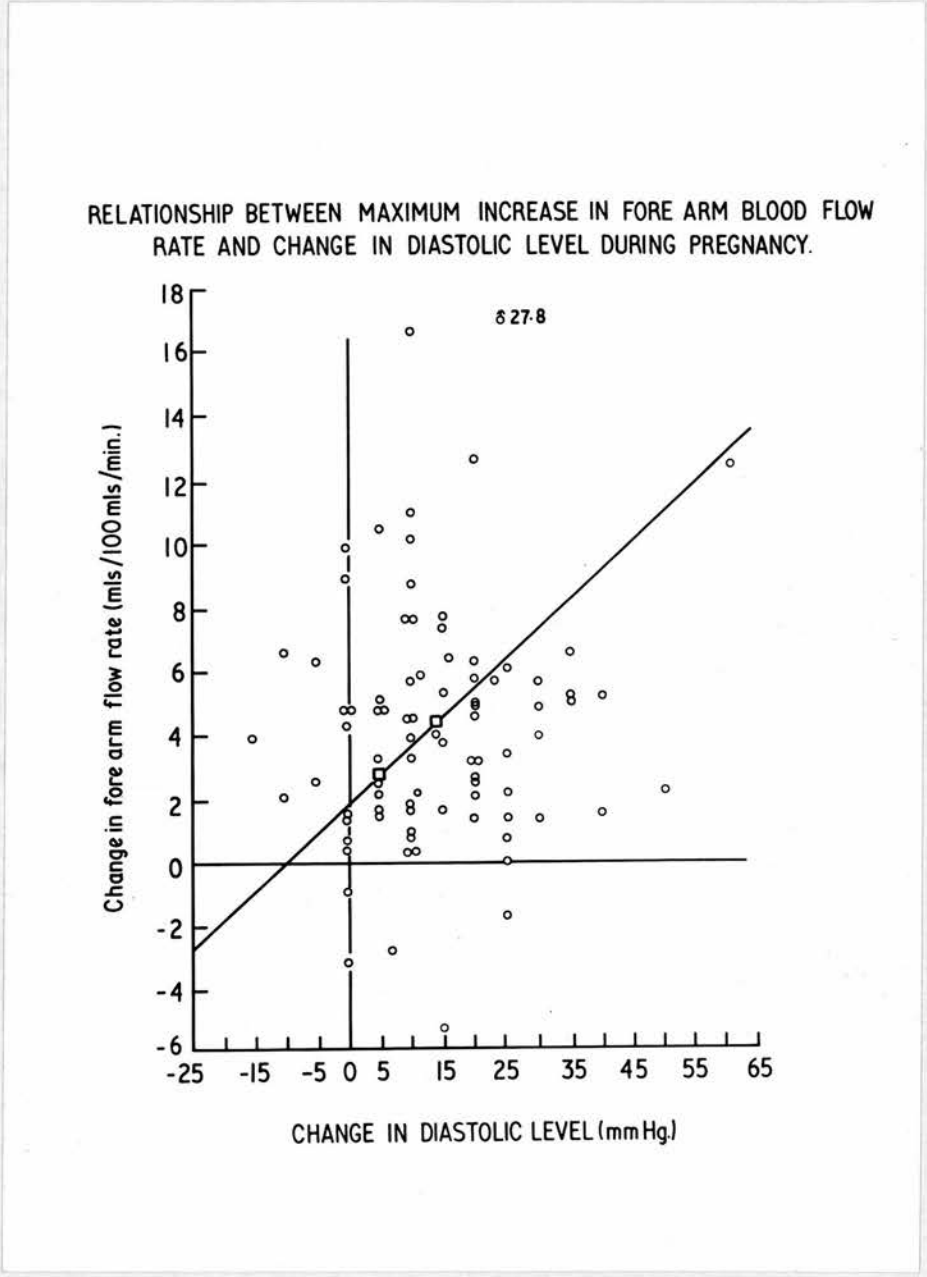



**Figure XIV**

Relationship between maximum increase in fore-arm blood flow rate and change in diastolic level during pregnancy. The regression line of flow on diastolic pressure is represented by open squares and a continuous line.

before delivery and the change in temperature gradient; t = 1.302 on 34 degrees of freedom, $0.3 > P > 0.2$.

5. The Relationship between Change in Antenatal Flow Rate and Change in Body Weight

There was no significant relationship between change in flow before delivery and increase in body weight; t = 1.576 on 77 degrees of freedom, $0.2 > P > 0.1$.

6. The Relationship between Fore-Arm Flow Rate and Birth Weight

There was no significant relationship between maximum change in flow rate before delivery and birth weight. For the normotensive group t = 1.100 on 24 degrees of freedom, $0.3 > P > 0.2$, for the hypertension I group t = 0.924 on 22 degrees of freedom, $0.4 > P > 0.3$, and for the hypertension II group t = 0.550 on 34 degrees of freedom, $0.6 > P > 0.5$.

7. The Relationship between Fore-Arm Blood Flow Rate and Pregnanediol Level (Figure XV)

There was a significant relationship between the change in fore-arm blood flow and the change in pregnanediol level from first visit to 32 - 35 weeks. A regression analysis gave b = -0.072; t = 2.702 on 31 degrees of freedom, $0.02 > P > 0.01$. A mean increase in pregnanediol level of 20 mg.% gave a mean increase in flow rate of 3.1 mls. per 100 mls./minute and a mean increase in pregnanediol level of 38.3 mg.% gave a mean increase in flow of 1.8 mls./100 mls./minute.

8. Relationship between Maximum Increase in Fore-Arm Flow and Change in Cornification Index (Figure XVI)

The greater the increase in flow rate the less is the decrease in cornification index; t = 2.764 on 84 degrees of freedom, $0.01 > P > 0.001$. Calculation of the regression gave b = +0.314. The mean change in cornification index was -2.63 $\pm$ S.D. 4.00 and the mean change in flow rate was +4.34 mls./100 mls./minute $\pm$ S.D. 4.35.

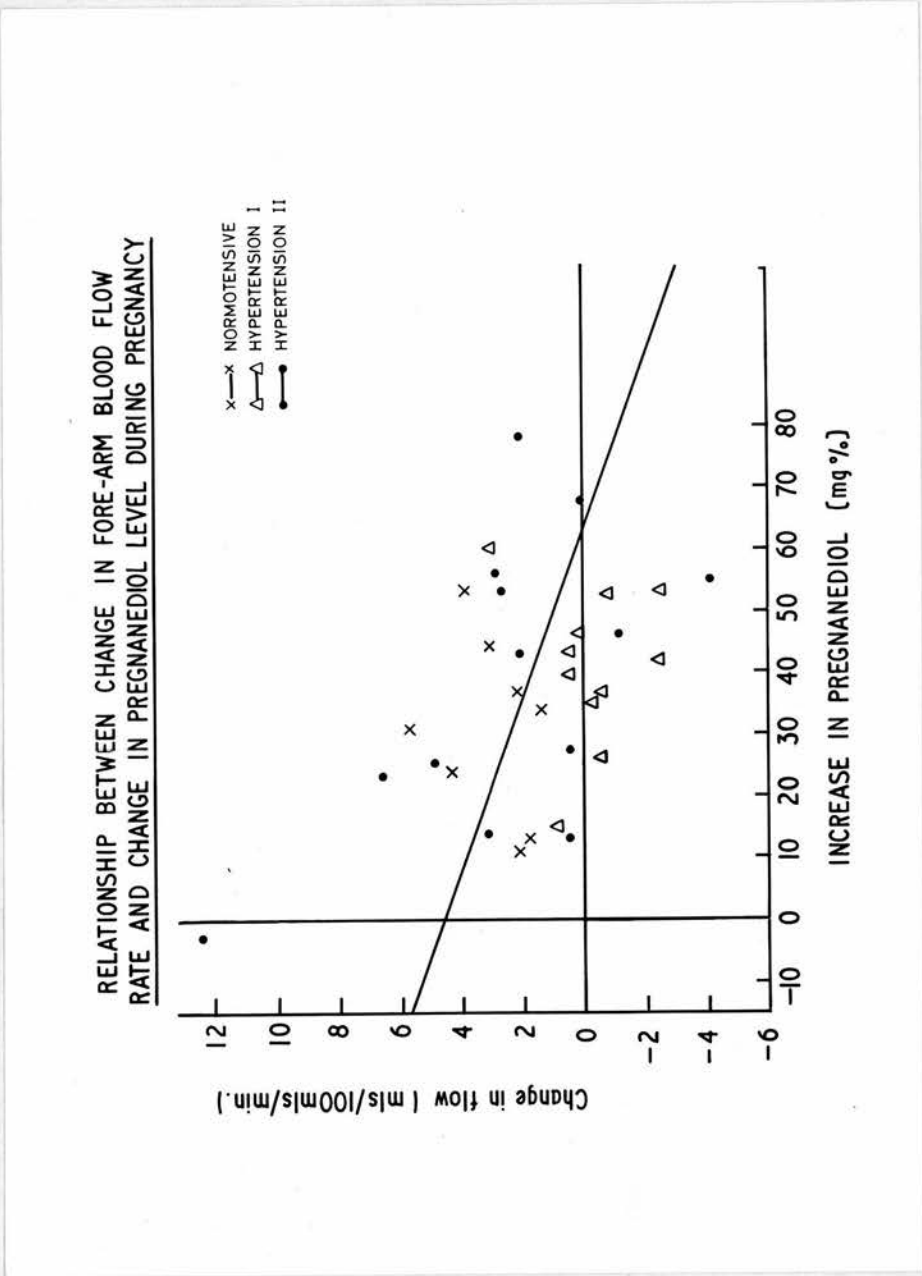



Figure XV

Relationship between change in fore-arm blood flow rate and change in pregnanediol level during pregnancy. The regression line of flow on pregnanediol excretion is represented by the continuous line.

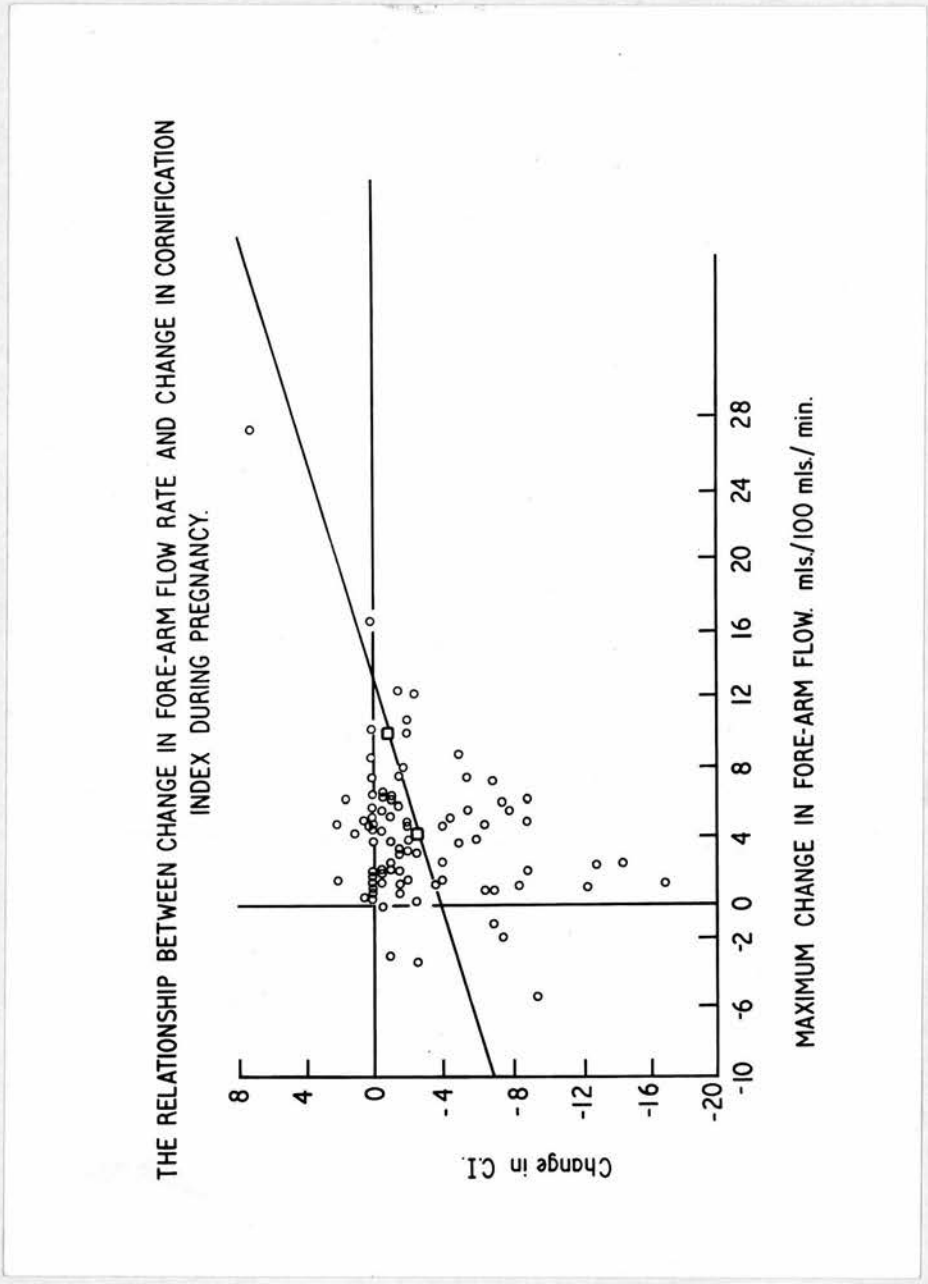



Figure XVI

Relationship between change in fore-arm flow rate and change in cornification index during pregnancy. The regression line of cornification index on flow is represented by the continuous line and open squares.

9. The Effect of Breast-Feeding, Resumption of Menstrual Cycle and Blood Pressure on Post-Natal Fore-Arm Blood Flow

An analysis of covariance was carried out on the mean fore-arm blood flow rates comparing subjects who were breast-feeding, artificially feeding, had resumed the menstrual cycle and not resumed a menstrual cycle for each blood pressure group. No significant differences were found between the groups. The menstrual cycle effect gave $F = 2.03$ on 1/7 degrees of freedom; the feeding effect gave $F = 0.52$ on 1/7 degrees of freedom and the blood pressure effect gave $F = 1.71$ on 2/7 degrees of freedom, $P > 0.05$ for all these F values.

Summary of Relationship of Fore-Arm Flow Rates in Experimental Group with Various Factors

1. The change in fore-arm blood flow rates during pregnancy increases with increasedin diastolic pressure.
2. The change in fore-arm blood flow rate in pregnancy increased with decreasing change in pregnanediol level.
3. The change in fore-arm blood flow rate increased with decreasing change in cornification index.
4. There was no relationship between fore-arm blood flow change and any of the following:

   (a) systolic pressure change
   (b) pulse rate change
   (c) blood volume change
   (d) change in temperature gradient
   (e) weight gain
   (f) birth weight
   (g) breast-feeding and artifical feeding
   (h) resumption of menstrual cycle.

## ABORTION AND FORE-ARM BLOOD FLOW

Four subjects aborted early in pregnancy. Their mean age was 25.0 years, range 20 to 31 years. Three were primigravidae and the fourth had one child. Two aborted before 12 weeks gestation and two aborted between 13 and 15 weeks gestation. All of the subjects were healthy. The mean haemoglobin level was 12.7 G.% ± S.D. 1.10.

In three subjects only one reading was obtained. In the fourth subject two readings were obtained before abortion. The mean fore-arm blood flow rate before abortion was 4.4 mls./100 mls./minute ± S.D. 0.9. This was highly significantly different from the mean first visit flow rate of the normotensive group mean which was 2.6mls. per 100 mls./minute; $t = 3.144$ on 24 degrees of freedom, $0.01 > P > 0.001$ and closely approximated the non-pregnant mean flow rate of 4.0 mls. per 100 mls./minute. The fourth subject showed an increase in flow rate, of 3.1 mls,/100 mls./minute from 8 - 11 weeks gestation (1.1 mls./100mls. per minute) to 12 - 15 weeks gestation.

Two of the subjects showed deficient progesterone effects on vaginal cytology, the cornification indices being 7 and 14 respectively. The other two subjects had good progesterone effects on vaginal cytology.

### Hydatidiform Mole and Fore-Arm Blood Flow Rates

One normotensive primigravid patient aged 18 years aborted a hydatidiform mole at 12 weeks gestation. A fore-arm flow reading was taken at 8 weeks gestation and was 2.1 mls./100 mls. per minute. This was not significantly different from the normotensive flow rate for the same period of gestation.

Accidental Ante-Partum Haemorrhage and Fore-Arm Flow Rates

One primigravid patient aged 26 years became pregnant while taking part in the control series. Four readings over a period of six months were obtained before pregnancy occurred. The mean pre-pregnancy flow rate was 2.6 mls./100 mls./minute ± S.D. 0.4. At 9 weeks gestation the mean flow rate was 9.0 mls./100 mls./minute. Thereafter the mean flow fell reaching its lowest level at 18 weeks gestation when it was 4.6 mls./100 mls./minute. A gradual rise succeeded this until at 39 weeks gestation the mean flow rate was 13.6 mls./100 mls./minute. At no time did the blood pressure exceed 130/80 mm.Hg. and this level was reached only once at 37 weeks gestation. The patient had an accidental ante-partum haemorrhage at 40 weeks gestation necessitating transfusion of 3 pints of blood and 1 pint of plasma. Delivery of a living 6 lb. 8½ oz. girl was by Caesarean Section. The total weight gain throughout pregnancy was 21.5 lbs. in 32 weeks and there were no signs of pre-eclampsia at any time. By twelve weeks after delivery the fore-arm flow rate was 3.3 mls./100 mls./minute. During this patient's second pregnancy we were able to estimate the fore-arm blood flow at 39 weeks gestation. Again, there was no sign of hypertension, oedema or excessive weight gain. The pregnancy was entirely normal throughout apart from a persistant breech presentation. The fore-arm flow rate at 39 weeks gestation was 3.0 mls./100 mls./minute which was within her pre-pregnancy range and 10.6 mls./100 mls./minute below the level reached at 39 weeks gestation in her previous pregnancy.

Fore-Arm Blood Flows in Twin Pregnancy complicated by hypertension and Oedema

A primigravid patient aged 25 years with a twin pregnancy was studied from 19 weeks gestation when the fore-arm blood flow rate was 11.2 mls./100 mls./minute. Her haemoglobin was 10.0 grammes at this time.

There was a gradual fall in flow rate until 35 weeks gestation when the rate was 2.4 mls./100 mls./minute. Hypertension and oedema first appeared at 30 weeks but were controlled by bed rest and mild sedation. The anaemia proved resistant to parenteral iron, folic acid and vitamin B12. At 37 weeks gestation, the fore-arm flow rate was 24.3 mls./100 mls./minute. At no time did the blood pressure exceed 150/98 mm.Hg. Labour was induced at 38 weeks gestation and she was delivered of twin male children weighing 6 lbs. 7½ ozs. and 6 lbs. 6½ ozs. respectively. On the fifth day following delivery the mean flow rate was 3.5 mls./100 mls./minute and at six weeks it was 2.7 mls./100 mls./minute which were slightly lower than the flow rates for the hypertension II group for the same time interval .

Fore-Arm Blood Flow Rates in a Patient who had Placental Insufficiency leading to Stillbirth in Early Labour

A primigravid patient aged 22 years was first seen at 10 weeks gestation with a history of threatened abortion at 7 weeks gestation. Her fore-arm flow rates at 10 weeks and 14 weeks gestation were 3.7 mls./100 mls./minute and 3.9 mls./100 mls./minute respectively, levels which approximated the mean non-pregnant level but were otherwise unremarkable. At 18 weeks gestation the flow rate was 2.1 mls./100 mls./minute. Thereafter it rose, reaching the maximum flow rate of 9.1 mls./100 mls./minute at 27 weeks gestation.

Following this there was a fall until 34 weeks when the flow rate was 6.0 mls./100 mls./minute. These flow rates were within the hypertensive groups range but outside that of the normotensive group. However, at no time did the blood pressure exceed 130/80 mm. Hg. a level which was recorded once only at 7 weeks gestation during the time that she had some bleeding vaginally. Apart from this,the blood pressure range was 110 - 140 mm. Hg. systolic over 60 to 78 mm. Hg. diastolic. There was no oedema. The total weight gain was 16 lbs. and 4 oz. in 27 weeks. At 37 weeks gestation spontaneous labour ensued and after 12 hours in poorly established labour the foetal heart beat disappeared. She was eventually delivered vaginally of a fresh stillborn foetus weighing 4 lbs. 12 ozs. after a course of buccal pitocin had been given. At post-mortem evidence of prolonged intra-uterine hypoxia and placental insufficiency was found.

At six weeks and 12 weeks after delivery the fore-arm flow rates were 3.1 mls./100 mls./minute and 3.8 mls./100 mls./minute respectively which were within the range of the non-pregnant control group levels.

Latent-Diabetes and Fore-Arm Blood Flows

A primigravid patient aged 23 years with a positive family history of diabetes proved to have latent-diabetes on investigation (Wright et al., 1968). The condition was controlled by diet during pregnancy. The total weight gain was 16.75 lbs. in 32 weeks. The blood pressure range was 105 - 130 mm. Hg. systolic over 60 - 80 mm. Hg. diastolic level. She was normotensive by the experimental criteria. Fore-arm blood flow rates during pregnancy behaved

erratically, high levels of 5.7 mls./100 mls./minute at 12 weeks gestation, 6.4 mls./100 mls./minute at 27 weeks gestation and 6.8 mls./100 mls./minute at 38 weeks gestation being attained. These levels are within the hypertensive experimental groups ranges. Labour was induced at 40 weeks and she had a normal delivery of a 9 pounds 1 oz. female infant after a 6 hour labour. Fore-arm blood flow rates at 12 weeks and 9 months after delivery were within the non-pregnant control group range, the flow at 9 months after delivery being 3.8 mls./100 mls./minute.

SUMMARY

Details have been given of four patients whose pregnancies ended in abortion, one patient who had a hydatidiform mole, one patient who had a severe accidental ante-partum haemorrhage, one patient who had placental insufficiency leading to stillbirth, one patient who had a twin pregnancy and one patient who had latent diabetes. (See Table 7 )

It has been shown that the mean fore-arm blood flow rate preceding abortion was significantly higher than the mean fore-arm blood flow for the normotensive group at the same period of gestation; a flow rate which equalled that of the non-pregnant control level. The fore-arm flow rate in the single case of hydatidiform mole did not differ from the normotensive flow rate for the same period. In the case of the severe accidental ante-partum haemorrhage and the case of stillbirth due to placental dysfunction very high fore-arm flow levels were found although both patients remained normotensive. That these levels were in fact abnormal are indicated by the fact

Table 7

Special Cases
Fore-Arm Flow Rates with Normotensive Pregnancy
Values for Comparison

| | Weeks | Normotensive Flow | | Abortion | | | | Mole | Accid. A.P.H. | Twins | S.B. | Latent Diabetes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | S.E. | Case 1 | Case 2 | Case 3 | Case 4 | | | | | |
| Pre-Pregnancy | 24 | | | | | | | | 2.4 | | | |
| | 8 | | | | | | | | 3.1 | | | |
| | 3 | | | | | | | | 2.4 | | | |
| Pregnancy | 1 | | | | | | | | 2.3 | | | |
| | 8 | 2.6 | 0.22 | 3.6 | 1.1 | 4.0 | 5.7 | 2.1 | 9.0 | - | 3.7 | 2.4 |
| | 12 | 3.2 | 0.37 | | 4.2 | | | | 5.4 | - | 3.9 | 5.7 |
| | 16 | 2.7 | 0.32 | | | | | | 4.6 | 11.2 | 2.1 | 4.0 |
| | 20 | 2.8 | 0.25 | | | | | | 6.3 | 6.0 | 4.6 | 2.0 |
| | 24 | 3.3 | 0.40 | | | | | | - | 3.9 | 9.1 | 6.4 |
| | 28 | 3.4 | 0.49 | | | | | | 7.3 | 4.3 | 7.9 | 2.8 |
| | 32 | 3.5 | 0.36 | | | | | | - | 2.4 | 6.0 | 4.8 |
| | 36 | 3.2 | 0.42 | | | | | | 13.6 | 24.3 | - | 6.8 |
| | 40 | 3.9 | 0.56 | | | | | | - | - | - | - |
| Post-Delivery | 3 days | 4.6 | 0.55 | | | | | | 7.6 | 3.5 | 5.1 | 6.3 |
| | 6 weeks | 3.1 | 0.26 | | | | | | - | 2.7 | 3.1 | 1.1 |
| | 12 weeks | 4.7 | 0.54 | | | | | | 3.3 | - | 3.8 | 2.0 |
| | 9 months | 4.1 | 0.53 | | | | | | - | - | - | 3.8 (16 weeks pregnant) |
| 2nd Pregnancy | 39 | | | | | | | | 3.0 | | | |

that pre-pregnancy flow rates and a flow rate taken in a subsequent pregnancy were within the normal range in the case of the patient with an accidental ante-partum haemorrhage. Very high fore-arm flow rates were also found in the patient with a twin pregnancy complicated by hypertension, oedema and anaemia and also in the case of the patient with latent diabetes who remained normotensive.

HAND BLOOD FLOW RATE

## HAND FLOW RATES

### The Control Group

#### Subjects

Fifteen non-pregnant subjects were examined on one occasion each. As fore-arm flow rates were reproducible over seven intervals it was thought that measurement of hand flow on one occasion per subject was sufficient to obtain a true non-pregnant control reading.

The mean age was 27.1 years ± S.D. 4.8 and the range was 21 to 34 years. All subjects were nulliparous. The mean height was 65.7 inches ± S.D. 2.6 and the mean weight was 136.4 lbs. ± S.D. 16.6. The mean surface area was 1.69 square metres ± S.D. 0.13.

#### Results

The mean flow rate for the 15 subjects was 9.2 mls./100 mls. per minute ± S.D. 4.27.

#### Age and Hand Flow Rates

No relationship could be found between the age of the subject and the hand flow rate; $t = 1.502$ on 13 degrees of freedom, $0.2 > P > 0.1$.

#### Parity and Hand Flow Rates

No parous patients were studied in the control group but there was no difference in mean hand flow rate of the control group and that of the six subjects examined at 12 weeks after delivery; $t = 0.304$ on 19 degrees of freedom, $0.8 > P > 0.7$.

#### The Relationship Between Body Surface Area and Hand Flow

No relationship was found between body surface area and hand flow rate; $t = 0.582$ on 13 degrees of freedom, $0.6 > P > 0.5$.

Smoking and Hand Flow Rates

Of the fifteen control subjects six smoked and nine did not. The mean hand flow rate for the smokers was 11.3 mls./100 mls. per minute ± S.D. 1.9 and that for the non-smokers was 7.71 mls./100 mls. per minute ± S.D. 4.9. There was no significant difference between the two; $t = 1.713$ on 13 degrees of freedom, $0.2 > P > 0.1$.

The Effect of the Menstrual Cycle on Hand Flow Rates

Hand flow rates were not measured in both stages of the cycle in the same patient but seven subjects were examined in the pre-ovulatory half of the cycle and eight subjects in the post-ovulatory phase. The mean hand flow rate for the pre-ovulatory phase was 11.5 mls./100 mls./minute ± S.D. 4.7 and that for the post-ovulatory phase was 7.1 mls./100 mls./minute ± S.D. 2.6. There was a significant decrease in flow in the second half of the cycle; $t = 2.278$ on 13 degrees of freedom, $0.05 > P > 0.02$.

Normal Body Temperature and Hand Blood Flow

No relationship was found between oral temperature and hand flow rate; $t = 1.429$ on 13 degrees of freedom, $0.2 > P > 0.1$.

Fore-Arm Skin Temperature and Hand Flow

It was not possible to measure ambient hand temperature during the experiment. The only skin temperature readings available are fore-arm temperatures measured on the same side as the hand flow. There was no relationship between fore-arm skin temperature and hand flow; $t = 0.804$ on 13 degrees of freedom, $0.5 > P > 0.4$.

Pulse Rate and Hand Flow

No relationship was demonstrable between pulse rate and hand flow; $t = 0.460$ on 13 degrees of freedom, $0.7 > P > 0.6$.

Pulse Pressure and Hand Flow

There was no relationship between pulse pressure and hand flow; $t = 1.186$ on 13 degrees of freedom, $0.3 > P > 0.2$.

Blood Pressure and Hand Flow

Nine of the control subjects were normotensive as defined by the experiment and the mean flow rate was 9.7 mls./100 mls./minute $\pm$ S.D. 5.3. Six subjects were hypertensive and the mean flow was 8.4 mls./100 mls./minute $\pm$ S.D. 2.4. There was no significant difference between the two groups; $t = 0.546$ on 13 degrees of freedom, $0.6 > P > 0.5$.

No relationship was found between systolic pressure and hand flow; $t = 0.564$ on 13 degrees of freedom, $0.6 > P > 0.5$; nor between diastolic pressure and hand flow; $t = 0.389$ on 13 degrees of freedom, $0.8 > P > 0.7$.

## Summary

1. There was a significant decrease in hand flow rates in the post-ovulatory phase of the menstrual cycle.
2. No significant relationship could be demonstrated between hand flow rates and the following parameters:

   (a) Age
   (b) Parity
   (c) Body Surface Area
   (d) Smoking habits
   (e) Normal body temperature
   (f) Pulse rate
   (g) Pulse pressure
   (h) Blood pressure

## Hand Flow Rates

| | | Non-Pregnant | Pregnant | Other Pregnant | Total |
|---|---|---|---|---|---|
| Number of Subjects | | 15 | 18 | 2 | 35 |
| Number of Readings | | 15 | 170 | 16 | 201 |
| Age (Years) | Mean | 27.1 | 22.3 | | |
| | S.D. | 4.8 | 2.4 | | |
| | Range | 21-34 | 19-28 | | |
| Parity | 0 | 15 | 14 | 2 | |
| | 1 | 0 | 4 | 0 | |
| | 2 & over | 0 | 0 | 0 | |
| Height (Inches) | Mean | 65.7 | 65.1 | | |
| | S.D. | 2.6 | 2.1 | | |
| Weight (lbs.) | Mean | 136.4 | 135.9 | | |
| | S.D. | 16.6 | 17.2 | | |
| Surface Area (Sq. metres) | Mean | 1.69 | 1.68 | | |
| | S.D. | 0.13 | 0.12 | | |
| Weight Gain (lbs.) | Mean | - | 21.8 | | |
| | S.D. | - | 7.3 | | |
| Birth Weight (grammes) | Mean | - | 3515 | - | |
| | S.D. | - | 418.7 | - | |

Table 8

## HAND FLOW RATES

### The Experimental Group

#### Subjects

Twenty subjects were examined on between 5 and 12 occasions each; a total of 186 readings were obtained. There were 3 subjects in the normotensive group, 6 subjects in the hypertension I group and 9 subjects in the hypertension II group. One subject had a twin pregnancy and another had a stillbirth. These last two subjects were excluded from the analysis and are discussed later. The numbers of subjects in each blood pressure group were small and as no significant difference was found in hand flows between the groups they were analysed as one group.

The mean age was 22.3 years ± S.D. 2.4 and the range was 19 years to 28 years. Fourteen subjects were primigravidae and the remainder had one child each. The mean height was 65.1 inches ± S.D. 2.1 and the mean weight at first visit was 135.87 lbs. ± S.D. 17.15. The mean surface area at first visit was 1.68 square metres ± S.D. 0.12. The mean birth weight was 3515 grammes ± S.D. 418.7.

#### Results

The mean hand flow rate with the standard deviation and standard error of the mean for each stage of gestation and period after delivery with t- values, degrees of freedom and P values for comparison with the non-pregnant group are enumerated in Table (9 ).

Table 9

Hand Flow Rates

| Weeks Gestation | Number of Subjects | Mean Flow Rate | S.D. | S.E. of Mean | Non-Pregnant Mean Flow Rate | t | Degrees of Freedom | P |
|---|---|---|---|---|---|---|---|---|
| 8 - 11 | 10 | 7.9 | 2.87 | 0.91 | 9.2 | | | |
| 12 - 15 | 12 | 7.9 | 3.24 | 0.94 | | 0.872 | 25 | 0.4 -0.3 |
| 16 - 19 | 17 | 11.7 | 6.50 | 1.58 | | 1.267 | 30 | 0.3 -0.2 |
| 20 - 23 | 18 | 14.8 | 5.91 | 1.40 | | 3.061 | 31 | 0.01-0.001 |
| 24 - 27 | 16 | 18.2 | 7.36 | 1.84 | | | | |
| 28 - 31 | 18 | 17.2 | 5.66 | 1.33 | | | | |
| 32 - 35 | 18 | 17.7 | 6.62 | 1.56 | | | | |
| 36 - 39 | 17 | 20.3 | 5.64 | 1.37 | | | | |
| 40 & over | 6 | 15.9 | 5.56 | 2.27 | | | | |
| (corrected) | | 18.7 | | | | | | |
| Post-Delivery | | | | | | | | |
| 3rd day | 17 | 16.0 | 5.60 | 1.36 | | | | |
| 6 weeks | 15 | 10.2 | 3.17 | 0.82 | | 0.729 | 28 | 0.5 -0.4 |
| 12 weeks | 6 | 8.6 | 3.51 | 1.43 | | | | |

There was a highly significant increase in hand flow during pregnancy. No significant change occurred between 8 - 11 weeks and 12 - 15 weeks gestation. A paired t-test gave a mean decrease of 0.5 mls./100 mls./minute $\pm$ S.D. 3.8; $t = 0.390$ on 7 degrees of freedom, $0.8 > P > 0.7$. A significant mean increase of 5.9 mls. per 100 mls./minute $\pm$ S.D. 5.3 occurred between 12 - 15 weeks and 16 - 19 weeks gestation; $t = 3.840$ on 11 degrees of freedom, $0.01 > P > 0.001$. Thereafter the hand flow rate increased rapidly, from first visit to 36 - 39 weeks gestation there was a significant increase of 11.9 mls./100 mls./minute $\pm$ S.D. 6.5; $t = 7.741$ on 17 degrees of freedom, $P < 0.001$.

In the six subjects who had flows estimated at 36 - 39 weeks gestation and 40 weeks gestation no significant change occurred. There was a mean decrease of 1.6 mls./100 mls./minute $\pm$ S.D. 5.3; $t = 0.721$ on 5 degrees of freedom, $0.6 > P > 0.5$. Therefore, no further increase in hand flow rate occurred after 36 - 39 weeks gestation.

The mean maximum increase in hand flow was 15.9 mls./100 mls per minute $\pm$ S.D. 6.7 and had occurred, on average, at 28 weeks gestation. A paired t-test gave $t = 10.150$ on 17 degrees of freedom, $P < 0.001$.

After delivery the mean hand flow rate had fallen by the third day by 4.3 mls./100 mls./minute from the 36 - 39 week level. This was a significant drop; $t = 2.726$ on 16 degrees of freedom, $0.2 > P > 0.01$. However, it was still significantly higher than the level at 12 - 15 weeks gestation by 7.8 mls./100 mls./minute; $t = 4.635$ on 11 degrees of freedom, $P < 0.001$.

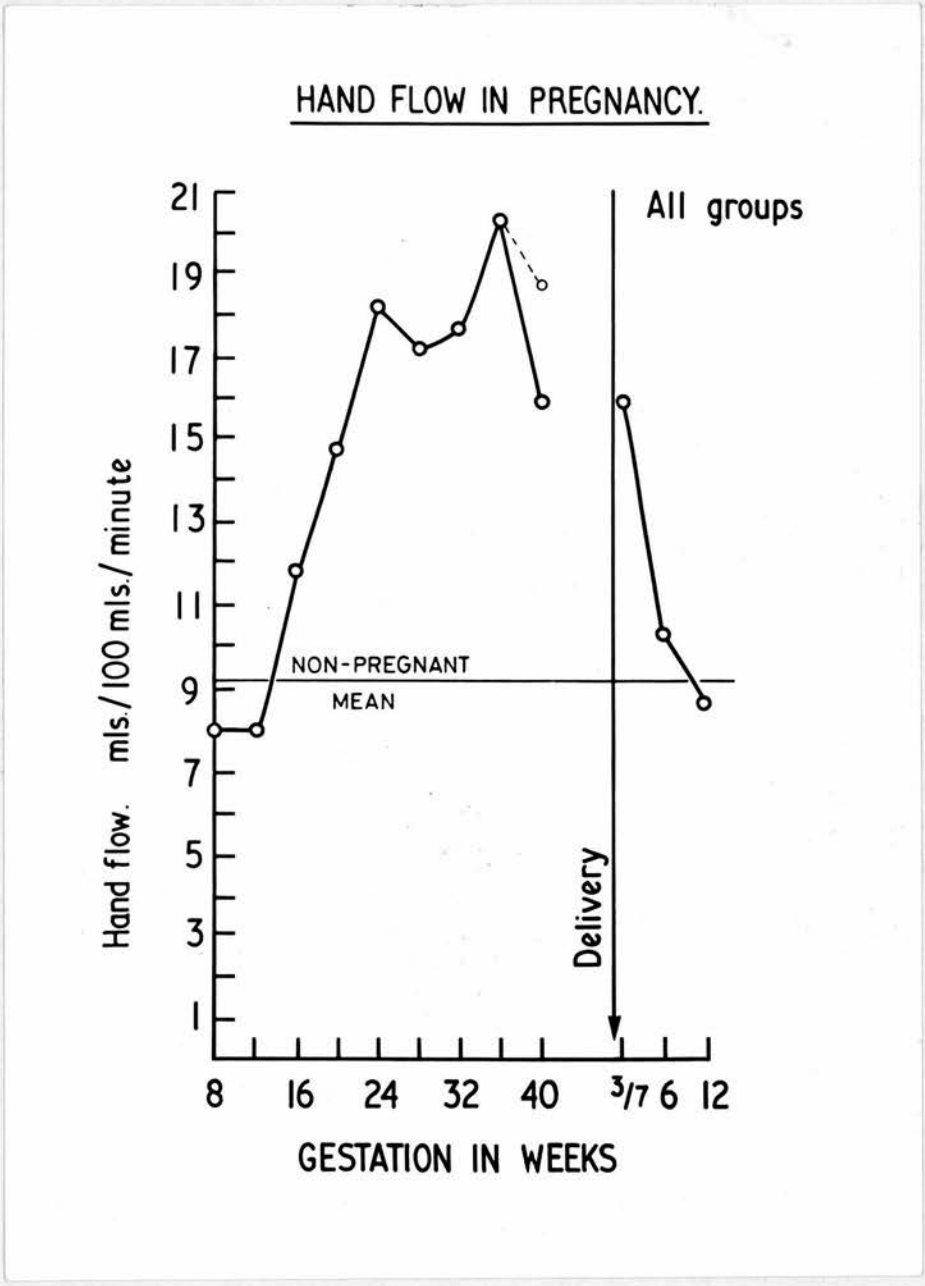



Figure XVII

Hand flow rates in pregnancy. The corrected reading is represented by the broken line.

The hand flow at six weeks after delivery was not significantly different from the flow rate at 12 - 15 weeks gestation; $t = 1.508$ on 10 degrees of freedom, $0.2 > P > 0.1$.

The Hand Flow rate of the Pregnant Group compared with the Non-Pregnant Control Group

The hand flow rate at 8 - 11 weeks and 12 - 15 weeks gestation did not differ significantly from the control group mean flow rate; $t = 1.267$ on 30 degrees of freedom, $0.3 > P > 0.2$. At 20 - 23 weeks gestation the flow was significantly higher than the non-pregnant group; $t = 3.061$ on 31 degrees of freedom, $0.01 > P > 0.001$; and became increasingly higher as pregnancy advanced. On the third post-natal day the flow rate was still higher than that of the control group but by six weeks after delivery the flow rate was again in the non-pregnant range; $t = 0.729$ on 28 degrees of freedom, $0.5 > P > 0.4$.

Blood Pressure and Hand Flow Rates in Pregnancy

The mean maximum increase in hand flow rate in the 3 normotensive group subjects during pregnancy was 11.5 mls./100 mls. per minute $\pm$ S.D. 4.7 and had occurred on average at 28 weeks gestation. The mean maximum increase in the six subjects in the hypertension I group was 20.0 mls./100 mls./minute $\pm$ S.D. 8.0 and had occurred by 31 weeks gestation. The mean maximum increase in flow in the 9 subjects in the hypertension II group was 14.6 mls./100 mls. per minute $\pm$ S.D. 5.2 and had occurred by 26 weeks gestation on average. Although there were differences in the maximum increase in hand flow of the three blood pressure groups the differences were not significant; for example between the normotensive and hypertension I groups

the difference was 8.5 mls./100 mls./minute but the numbers are small and the ranges wide; t = 1.672 on 7 degrees of freedom, $0.2 > P > 0.1$.

There was no relationship between the maximum increase in hand flow and the maximum change in systolic pressure; t = 0.268 on 16 degrees of freedom, $0.8 > P > 0.7$. There was no relationship between the maximum increase in hand flow and the maximum change in diastolic pressure; t = -0.638 on 16 degrees of freedom, $0.6 > P > 0.5$.

Change in Hand Flow and Change in Pulse Rate

There was no relationship between the maximum change in hand flow rate and change in pulse rate during pregnancy; t = 2.012 on 16 degrees of freedom, $0.1 > P > 0.05$.

Increase in Hand Flow and Parity

From first visit to 36 - 39 weeks gestation there was a mean increase in flow rate of 11.0 mls./100 mls./minute $\pm$ S.D. 6.1 in the primigravid patients and a mean increase of 15.3 mls./100 mls. per minute $\pm$ S.D. 7.8 in the parous patients. There was no significant difference between the two groups; t = 1.176 on 16 degr es of freedom, $0.1 > P > 0.05$.

Smoking Habits and Hand Flow

The mean hand flow rates for the 7 smokers and 10 non-smokers at first visit were 7.9 mls./100 mls./minute $\pm$ S.D. 2.6 and 8.0 mls. per 100 mls./minute $\pm$ S.D. 4.2 respectively. The increase in flow rate from first visit to 36 - 39 weeks gestation in smokers and non-smokers was 12.5 mls./100 mls./minute $\pm$ S.D. 7.1 and 11.9 mls. per 100 mls./minute $\pm$ S.D. 2.2 respectively; t = 0.457 on 15 degrees of freedom, $0.7 > P > 0.6$.

Change in Hand Flow and Change in Body Weight

There was no relationship between the maximum change in hand flow rate and the total weight gain during pregnancy; $t = -1.624$ on 16 degrees of freedom, $0.2 > P > 0.1$.

Change in Hand Flow and Birth Weight

There was no relationship between the maximum change in hand flow rate and birth weight; $t = 0.916$ on 16 degrees of freedom, $0.4 > P > 0.3$.

Change in Hand Flow Rate and Change in Body Temperature

No relationship could be demonstrated between the maximum change in hand flow rate and the change in body temperature during pregnancy; $t = 0.256$ on 16 degrees of freedom, $0.9 > P > 0.8$.

Hand Flow Rates in Twin Pregnancy

The details of this patient have been discussed on page 91. No recordings were made before 16 weeks gestation when the hand flow rate was 36.7 mls./100 mls./minute which was well beyond the 11.7 $\pm$ S.D. 6.5 mls./100 mls./minute for this stage in pregnancy. However, for the remainder of the pregnancy the hand flow rates were within one standard deviation of the mean for the pregnant group.

Hand Flow Rates in Pregnancy Resulting in Stillbirth

The details of this patient were discussed on page 91. Throughout pregnancy the hand flow rates were within the standard deviation of the mean for the pregnant group.

## Summary of Hand Flow Rates in Pregnancy and up to Twelve Weeks after Delivery

There was no significant difference in the behaviour of the normotensive and hypertensive groups. This may have been due to the fact that there were very small numbers in each group. The remaining analysis was carried out on all subjects as one group.

There was no change in the first two intervals in pregnancy and the mean flow rate was not significantly different from the control group mean.

A significant increase in flow began between 12 - 15 weeks gestation but there was still no significant difference from the control group mean.

After 16 weeks gestation the hand flow increased rapidly to 36 - 39 weeks gestation after which there was a slight and insignificant fall.

By the third day after delivery the hand flow rate had fallen significantly but remained significantly higher than the first visit flow rate.

From 6 weeks after delivery the hand flow rate was within non-pregnant control levels and did not differ from the first visit levels.

No relationship could be demonstrated between change in hand flow rates and parity, smoking habits, change in blood pressure, change in pulse rate, change in body weight, change in body temperature or birth weight.

Apart from one reading in early pregnancy all the hand flow rates in a twin pregnancy studied were within the normal range for the pregnant group. The hand flow rates recorded in one subject who

had a stillbirth due to placental insufficiency were within the normal range for each stage of pregnancy.

## The Relationship Between Fore-Arm and Hand Flows

### The Control Group

Hand and fore-arm flow rates were measured simultaneously in 15 subjects. The mean fore-arm flow rate was 4.8 mls./100 mls. per minute ± S.D. 2.1 and the mean hand flow rate was 9.2 mls./100 mls. per minute ± S.D. 4.3. The mean difference between the two rates was 4.3 mls./100 mls./minute ± S.D. 5.2; that is, the rate of hand flow was 89.6% higher than the fore-arm flow rate.

### The Pregnant Group

At twelve to fifteen weeks gestation the mean fore-arm flow rate was 3.7 mls./100 mls./minute ± S.D. 1.8 and the mean hand flow taken at the same time was 7.9 mls./100 mls./minute ± S.D. 3.2. The mean difference was 4.4 mls./100 mls./minute ± S.D. 3.8, that is, the hand flow rate was 118.2% greater than the corresponding fore-arm flow rate.

At 36 - 39 weeks gestation the mean fore-arm flow rate was, 6.9 mls./100 mls./minute ± S.D. 6.4 and the corresponding mean hand flow rate was 20.3 mls./100 mls./minute ± S.D. 5.6. The mean difference was 13.6 mls./100 mls./minute ± S.D. 7.9, that is, the hand flow rate was 197.3% greater than the corresponding arm flow rate.

There is increasing disparity between hand and fore-arm flow rates measured simultaneously during pregnancy until at 36 - 39 weeks gestation the disparity is more than twice as great as the non-pregnant level.

(N.B. The fore-arm flow rate means are high because 15 of the 18 subjects in the pregnant group would have been included in the hypertensive groups.)

Other Circulatory Changes

## THE BLOOD PRESSURE AT THE TIME OF MEASUREMENT OF FORE-ARM BLOOD FLOW

### The Control Group

Twenty-two subjects were normotensive as previously defined. The mean blood pressure was calculated for each subject to calculate the mean blood pressure for the group. The mean systolic pressure was 113.2 mm. Hg. ± S.D. 7.2 and the mean diastolic pressure was 68.1 mm. Hg. ± S.D. 6.3.

Ten subjects were hypertensive as defined. The mean systolic pressure was 127.7 mm Hg. ± S.D. 7.1 and the mean diastolic pressure was 80.4 mm. Hg. ± S.D. 5.3. The differences in blood pressure between the two groups were highly significant. For systolic pressures $t = 5.333$ on 30 degrees of freedom, $P < 0.001$; and for diastolic pressures $t = 5.356$ on 30 degrees of freedom, $P < 0.001$.

The mean systolic pressure for all control subjects was 117.7 mm Hg. ± S.D. 9.8 and the mean diastolic pressure was 72.0 mm. Hg. ± S.D. 8.3.

Reproducibility Between Intervals (Table 10)

Nine of the normotensive subjects had blood pressures recorded in each of six intervals. From first to second intervals there was a mean decrease in systolic pressure of 2.8 mm. Hg. ± S.D. 13.8; $t = 0.609$ on 8 degrees of freedom, $0.6 > P > 0.5$; and a mean decrease in diastolic pressure of 2.2 mm. Hg. ± S.D. 9.7; $t = 0.679$ on 8 degrees of freedom, $0.6 > P > 0.5$. From first to sixth intervals there was a mean decrease in systolic pressure of 8.1 mm. Hg. ± S.D. 12.9; $t = 1.882$ on 8 degrees of freedom, $0.1 > P > 0.05$; and

Table 10

## Blood Pressure at Time of Measurement of Fore-Arm Flow Rate
## Reproducibility Between Intervals

| Subjects | Intervals | | | | | | Intervals | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 1 | 2 | 3 | 4 | 5 | 6 |
| | SYSTOLIC PRESSURE | | | | | | DIASTOLIC PRESSURE | | | | | |
| Normotensive: | | | | | | | | | | | | |
| No. 1 | 120 | 100 | 100 | 110 | 105 | 120 | 80 | 60 | 60 | 70 | 50 | 70 |
| No. 2 | 115 | 130 | 110 | 110 | 100 | 110 | 70 | 80 | 75 | 80 | 70 | 70 |
| No. 3 | 108 | 110 | 110 | 120 | 118 | 110 | 60 | 70 | 80 | 60 | 70 | 65 |
| No. 4 | 140 | 110 | 110 | 100 | 110 | 100 | 80 | 70 | 70 | 50 | 60 | 60 |
| No. 5 | 120 | 120 | 115 | 110 | 100 | 110 | 80 | 70 | 70 | 60 | 70 | 70 |
| No. 6 | 110 | 118 | 110 | 105 | 110 | 110 | 70 | 70 | 75 | 70 | 70 | 60 |
| No. 7 | 120 | 120 | 110 | 120 | 100 | 120 | 70 | 70 | 80 | 75 | 60 | 80 |
| No. 8 | 110 | 110 | 120 | 110 | 105 | 100 | 70 | 70 | 70 | 70 | 70 | 55 |
| No. 9 | 120 | 120 | 120 | 112 | 120 | 110 | 70 | 70 | 60 | 60 | 60 | 70 |
| Mean | 118.1 | 115.3 | 111.7 | 110.8 | 107.6 | 110.0 | 72.2 | 70.0 | 71.1 | 66.1 | 64.4 | 66.7 |
| S.D. | 9.60 | 8.72 | 6.12 | 6.36 | 7.58 | 7.07 | 6.67 | 5.00 | 7.41 | 9.28 | 7.26 | 7.50 |
| Hypertensive: | | | | | | | | | | | | |
| No. 1 | 130 | 136 | 140 | 130 | 130 | 125 | 86 | 86 | 86 | 90 | 86 | 70 |
| No. 2 | 136 | 126 | 120 | 130 | 130 | 120 | 86 | 80 | 80 | 76 | 60 | 76 |
| No. 3 | 120 | 130 | 120 | 120 | 120 | 110 | 75 | 80 | 80 | 80 | 70 | 70 |
| No. 4 | 150 | 120 | 120 | 118 | 120 | 110 | 80 | 80 | 70 | 76 | 76 | 76 |
| No. 5 | 135 | 130 | 110 | 130 | 110 | 100 | 80 | 70 | 75 | 80 | 70 | 60 |
| Mean | 134.2 | 128.4 | 122.0 | 125.6 | 122.0 | 113.0 | 81.4 | 79.2 | 78.2 | 80.4 | 72.4 | 70.4 |
| S.D. | 10.87 | 5.90 | 10.95 | 6.07 | 8.37 | 9.75 | 4.67 | 5.76 | 6.02 | 5.73 | 9.53 | 6.54 |

a mean decrease in diastolic pressure of 5.6 mm. Hg. ± S.D. 9.8; $t = 1.071$ on 8 degrees of freedom, $0.4 > P > 0.3$.

Five of the hypertensive subjects had blood pressures recorded in each of six intervals. From the first to the second interval there was a mean decrease in systolic level of 5.8 mm. Hg. ± S.D. 15.8; $t = 0.823$ on 4 degrees of freedom, $0.5 > P > 0.4$; and a mean decrease in diastolic pressure of 2.2 mm. Hg. ± S.D. 5.9; $t = 0.841$ on 4 degrees of freedom, $0.5 > P > 0.4$. From first to sixth intervals there was a mean decrease in systolic pressure of 21.2 mm. Hg. ± S.D. 15.5; $t = 3.062$ on 4 degrees of freedom, $0.05 > P > 0.02$. There was a mean decrease in diastolic pressure of 11.0 mm. Hg. ± S.D. 6.9; $t = 3.550$ on 4 degrees of freedom, $0.05 > P > 0.02$.

In summary, neither the normotensive group nor the hypertensive group showed a significant fall in blood pressure from first to second intervals and the decrease from first to sixth intervals was only significant in the hypertensive group.

## The Normotensive Group

Throughout pregnancy no significant change occured in blood pressure in this group; $t = 0.861$ on 24 degrees of freedom, $0.4 > P > 0.3$ for change in systolic pressure and $t = 1.419$ on 24 degrees of freedom, $0.2 > P > 0.1$ for change in diastolic pressure.

The mean systolic and diastolic pressures with the standard deviation and standard error of the means are given in Table (11 ).

On the third day after delivery the mean blood pressure was significantly higher than at first visit. Paired t-test on systolic pressures gave $t = 2.718$ on 25 degrees of freedom, $0.02 > P > 0.01$ and on diastolic pressure gave $t = 4.856$ on 25 degrees of freedom, $P < 0.001$.

## Blood Pressure at Time of Flow Readings

| Weeks Gestation | Number of Subjects | Mean Systolic Pressure | S.D. | S.E. | Mean Diastolic Pressure | S.D. | S.E. |
|---|---|---|---|---|---|---|---|
| **NORMOTENSIVE GROUP** | | | | | | | |
| 8 - 11 | 22 | 118.0 | 11.78 | 2.51 | 65.9 | 5.59 | 1.19 |
| 12 - 15 | 26 | 118.8 | 9.07 | 1.78 | 66.8 | 5.95 | 1.17 |
| 16 - 19 | 25 | 117.7 | 10.11 | 2.02 | 65.2 | 5.91 | 1.18 |
| 20 - 23 | 25 | 119.6 | 11.08 | 2.22 | 66.6 | 5.96 | 1.19 |
| 24 - 27 | 26 | 119.7 | 11.75 | 2.30 | 66.3 | 6.25 | 1.23 |
| 28 - 31 | 26 | 118.8 | 10.65 | 2.09 | 66.5 | 6.45 | 1.26 |
| 32 - 35 | 26 | 117.2 | 8.68 | 1.70 | 70.0 | 8.12 | 1.59 |
| 36 - 39 | 25 | 115.6 | 10.26 | 2.05 | 68.8 | 7.03 | 1.41 |
| 40 & over | 11 | 116.4 | 8.09 | 2.44 | 68.5 | 7.89 | 2.38 |
| (corrected) | | 116.1 | | | 69.6 | | |
| Post-Delivery | | | | | | | |
| 3rd day | 26 | 125.1 | 10.09 | 2.14 | 75.3 | 7.47 | 1.46 |
| 6 weeks | 26 | 121.7 | 13.03 | 2.56 | 72.0 | 8.39 | 1.65 |
| 12 weeks | 24 | 117.7 | 12.68 | 2.59 | 70.8 | 6.56 | 1.34 |
| 9 months | 15 | 117.7 | 13.74 | 3.55 | 66.3 | 9.35 | 2.41 |
| (corrected) | | 113.4 | | | 61.1 | | |
| **HYPERTENSION I GROUP** | | | | | | | |
| 8 - 11 | 22 | 129.3 | 14.17 | 3.02 | 74.2 | 7.58 | 1.62 |
| 12 - 15 | 23 | 128.0 | 11.85 | 2.47 | 74.6 | 8.65 | 1.80 |
| 16 - 19 | 24 | 130.2 | 8.01 | 1.64 | 76.4 | 7.74 | 1.58 |
| 20 - 23 | 24 | 125.0 | 14.14 | 2.88 | 72.3 | 8.09 | 1.65 |
| 24 - 27 | 24 | 128.5 | 10.95 | 2.24 | 74.1 | 5.96 | 1.22 |
| 28 - 31 | 24 | 128.9 | 9.32 | 1.90 | 76.3 | 7.49 | 1.53 |
| 32 - 35 | 24 | 129.5 | 9.44 | 1.93 | 79.4 | 7.39 | 1.51 |
| 36 - 39 | 24 | 126.3 | 11.46 | 2.34 | 79.2 | 7.89 | 1.61 |
| 40 & over | 11 | 134.1 | 10.20 | 3.08 | 84.1 | 7.01 | 2.11 |
| (corrected) | | 133.0 | | | 84.6 | | |
| Post-Delivery | | | | | | | |
| 3rd day | 24 | 129.5 | 15.19 | 3.10 | 77.8 | 11.77 | 2.40 |
| 6 weeks | 23 | 128.7 | 13.92 | 2.90 | 80.2 | 10.72 | 2.24 |
| 12 weeks | 18 | 127.1 | 14.00 | 3.30 | 75.7 | 8.40 | 1.98 |
| 9 months | 10 | 126.0 | 12.65 | 4.00 | 76.1 | 6.74 | 2.13 |
| (corrected) | | 129.5 | | | 76.3 | | |

Table 11

Hypertension II Group

Blood Pressure at the Time of Flow Readings

| Weeks Gestation | Number of Subjects | Mean Systolic Pressure | S.D. | S.E. | Mean Diastolic Pressure | S.D. | S.E. |
|---|---|---|---|---|---|---|---|
| 8 - 11 | 30 | 119.3 | 13.24 | 2.42 | 66.5 | 6.36 | 1.16 |
| 12 - 15 | 33 | 119.6 | 11.41 | 1.99 | 65.8 | 6.55 | 1.14 |
| 16 - 19 | 34 | 123.6 | 10.92 | 1.87 | 67.3 | 6.03 | 1.03 |
| 20 - 23 | 35 | 121.0 | 12.10 | 2.05 | 69.1 | 6.77 | 1.14 |
| 24 - 27 | 35 | 125.8 | 8.78 | 1.48 | 70.5 | 7.95 | 1.34 |
| 28 - 31 | 36 | 124.2 | 11.72 | 1.95 | 72.0 | 9.49 | 1.58 |
| 32 - 35 | 36 | 123.1 | 10.53 | 1.76 | 74.7 | 7.43 | 1.24 |
| 36 - 39 | 36 | 127.3 | 12.65 | 2.11 | 80.1 | 7.32 | 1.22 |
| 40 & over | 23 | 127.3 | 10.75 | 2.24 | 79.7 | 7.76 | 1.62 |
| (corrected) | | 128.7 | | | 79.4 | | |
| Post Delivery | | | | | | | |
| 3rd day | 36 | 126.0 | 12.60 | 2.10 | 78.1 | 8.30 | 1.38 |
| 6 weeks | 33 | 125.6 | 9.47 | 1.65 | 75.6 | 7.52 | 1.31 |
| 12 weeks | 27 | 128.2 | 13.81 | 2.66 | 74.6 | 8.87 | 1.71 |
| 9 months | 14 | 121.5 | 6.96 | 1.86 | 69.9 | 8.82 | 2.36 |
| (corrected) | | 124.7 | | | 70.5 | | |

Table 11 cont.

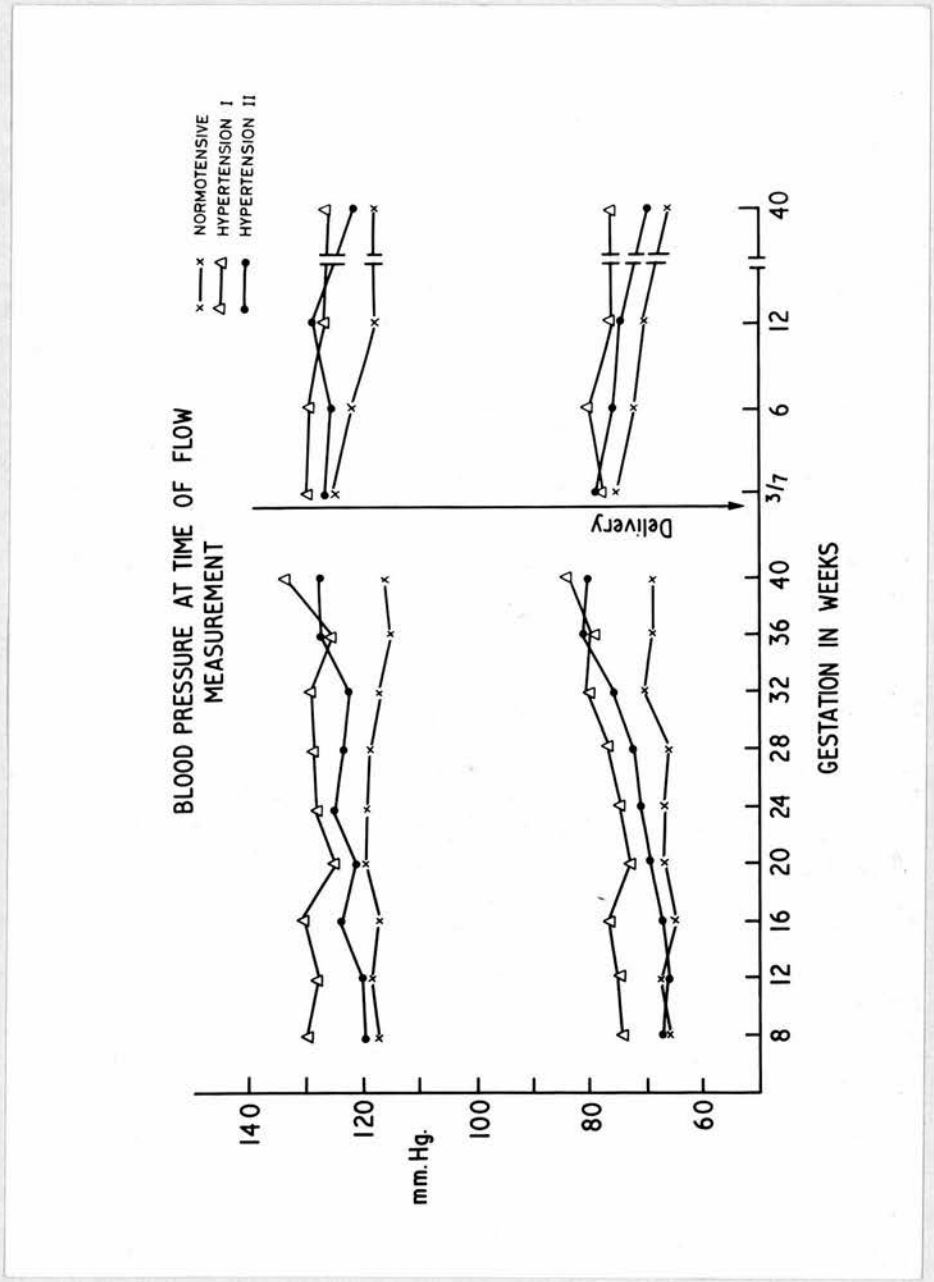



Figure XVIII

Blood pressure at time of blood flow measurement.

Following this there was a fall in blood pressure and at 12 weeks after delivery the systolic pressure had fallen to first visit levels; $t = 0.337$ on 23 degrees of freedom, $0.8 > P > 0.7$, but the diastolic pressure was still significantly raised; $t = 2.788$ on 23 degrees of freedom, $0.02 > P > 0.01$.

By nine months after delivery both systolic and diastolic pressures had reached first visit levels.

Comparison with Normotensive Control Group

At 8 weeks gestation there was no significant difference in systolic or diastolic pressures from the non-pregnant normotensive control group. For systolic pressure $t = 1.633$ on 42 degrees of freedom, $0.2 > P > 0.1$ and for diastolic pressure $t = 1.252$ on 42 degrees of freedom, $0.3 > P > 0.2$.

Reproducibility Between the First Two Intervals

There was no difference in the mean blood pressures taken at 8 - 11 weeks and 12 - 15 weeks gestation.

## The Hypertension I Group

No significant change occurred in the systolic pressure at any stage. A paired t-test between readings taken at first visit and 36 - 39 weeks gestation gave $t = 0.861$ on 23 degrees of freedom, $0.4 > P > 0.3$. The mean systolic and diastolic pressures with the standard deviation and standard error are given in Table ( ).

The diastolic pressure altered significantly from first visit to 36 weeks gestation by an increase of 4.2 mm. Hg. $\pm$ S.D. 12.2 on average; $t = 2.494$ on 23 degrees of freedom, $0.05 > P > 0.02$. On the third day after delivery it was still raised but by 12 weeks

after delivery there was no significant difference from the first visit level.

Comparison with the Hypertensive Control Group

At 8 - 11 weeks gestation there was no difference between the systolic pressure of the pregnant group and that of the non-pregnant hypertensive control group but the diastolic level was significantly lower than that of the non-pregnant group by 6 mm. Hg.; $t = 2.328$ on 30 degrees of freedom, $0.05 > P > 0.02$.

Reproducibility Between the First Two Intervals

There was no difference in mean blood pressure between 8 - 11 weeks gestation and 12 - 15 weeks gestation.

## The Hypertension II Group

The mean systolic and diastolic pressures with the standard deviations and standard errors of the means for each interval are given in Table ( 11).

The blood pressure rose significantly from 119.3/66.5 mm. Hg. at 8 - 11 weeks gestation to 127.3/80.1 mm. Hg. at 36 - 39 weeks gestation. A paired t-test for systolic pressures gave $t = 2.395$ on 35 degrees of freedom, $0.05 > P > 0.02$, and for diastolic pressures $t = 7.316$ on 35 degrees of freedom, $P < 0.001$. The blood pressure remained significantly elevated after delivery. Comparing 12 weeks after delivery with first visit levels, a paired t-test on systolic pressures gave $t = 2.679$ on 26 degrees of freedom, $0.02 > P > 0.01$ and on diastolic pressures $t = 3.617$ on 26 degrees of freedom, $0.01 > P > 0.001$.

At forty weeks after delivery there was no significant difference from the first visit blood pressure.

Comparison with the Normotensive Control Group

There was no difference between the mean blood pressure for the normotensive non-pregnant control group and that for the hypertension II group at 8 - 11 weeks gestation.

Reproducibility in the First Two Intervals

There was no difference between the blood pressures from 8 - 11 weeks to 12 - 15 weeks gestation.

The Relationship Between the Blood Pressures Recorded at the Time of Flow Readings for Each Experimental Group

As defined in the experiment there was a significant difference between the blood pressures recorded in the normotensive and hypertension I groups in early pregnancy and a significant difference was apparent from the first visit. At 8 - 11 weeks gestation the mean blood pressure of the hypertension I group was 11.3/8.3 mm. Hg. higher than the mean normotensive blood pressure. For the difference in diastolic pressure t was 4.136 on 42 degrees of freedom, $P < 0.001$. This significant difference was maintained throughout pregnancy.

At 8 - 11 weeks gestation there was no indication of the eventual difference between the hypertensive II group and the normotensive group, the mean blood pressures being almost identical. The first indication of an eventual difference was a significant rise in systolic pressure at 16 - 19 weeks gestation in the hypertensive II group; $t = 2.116$ on 57 degrees of freedom, $0.05 > P > 0.02$. The diastolic pressure did not become significantly different between the two groups until 24 - 27 weeks gestation; $t = 2.228$ on 59 degrees of freedom, $0.05 > P > 0.02$.

It was notable that the greatest differences occurred in the diastolic pressures rather than the systolic pressures.

No significant change in diastolic or systolic level occurred during pregnancy in the normotensive and hypertension I groups but a significant change occurred in the hypertensive II groups as the blood pressure level rose during pregnancy from the level of the normotensive group to the level of the hypertension I group.

After delivery both the normotensive and hypertension I group mean blood pressures were back to their respective first visit levels by 12 weeks but the blood pressure of the hypertension II group had not reached first visit levels until 9 months after delivery.

Highest Blood Pressure Recorded in Each Interval

Every blood pressure recorded on every subject during pregnancy and the post-natal period was tabulated and inspected before allotting a patient to any of the experimental groups. For clarity the data have been tabulated as the highest blood pressure recorded in each interval and to obtain the most complete overall view a column for blood pressure recorded during labour and the immediate post-partum 24 hours was added and the column for 3rd day after delivery was expanded to include the highest blood pressure recorded in the period from 24 hours after delivery to the time of the patients' discharge from hospital.

This method of presentation takes little account of the number of times a particular reading was obtained nor of the period over which it was sustained, nor does it gave a true picture of the

range of blood pressure. The lowest blood pressures recorded for each patient are more nearly represented in the table of blood pressures recorded at the time of flow reading sessions and it is from a study of both of these tables that the best picture can be obtained.

Blood pressure readings taken during other pregnancies and other hospital attendances for non-obstetrical reasons were also collected from the hospital notes but no account of these was taken in allotting a patient to any of the experimental groups as this information was available for only a proportion of patients and it was felt a bias might be introduced into the experiment. However, it was found that most patients in whom blood pressures had been recorded over 120/80 mm. Hg. on occasions other than the pregnancy and puerperium under study, did, in fact, fall into the hypertension I group.

In the first half of pregnancy only the blood pressure taken at the time of flow reading was recorded in any interval unless the patient showed early signs of hypertension or visited the hospital more frequently for some other complication. Similarly, from 6 weeks after delivery only those blood pressures recorded at the time of flow readings were available for each interval.

## The Highest Blood Pressure Recorded in Each Experimental Interval

### The Normotensive Group

There was a significant rise in both systolic and diastolic pressures from the first visit to 36 - 39 weeks gestation. The systolic level rose by a mean of 5.8 mm. Hg. ± S.D. 12.2; $t = 2.385$ on 24 degrees of freedom, $0.05 > P > 0.02$. The diastolic level rose by a mean of 8.4 mm.Hg. ± S.D. 10.2; $t = 3.944$ on 24 degrees of freedom, $P < 0.001$.

A further increase occurred during labour giving a mean rise in systolic level of 8.1 mm. Hg. ± S.D. 14.2 from first visit; $t = 2.903$ on 25 degrees of freedom, $0.01 > P > 0.001$; and a mean rise in diastolic level of 15.4 mm. Hg. ± S.D. 13.2 from first visit; $t = 5.958$ on 25 degrees of freedom, $P < 0.001$. In the period from 24 hours after delivery to discharge from hospital (usually 7th to 8th day post-partum) the mean increase over first visit levels was 9.8 mm. Hg. ± S.D. 9.7 for the systolic pressure and 15.3 mm. Hg. ± S.D. 7.6 for the diastolic pressure ; $P < 0.001$ for both increases.

Thereafter, the blood pressure fell to first visit levels. This degree of change in blood pressure during pregnancy did not occur in the blood pressures recorded at the time of measurement of fore-arm flow rates.

### The Hypertension I Group

There was a significant rise in both systolic and diastolic pressures from the first visit to 36 - 39 weeks gestation. The systolic pressure rose by a mean of 9.0 mm. Hg. ± S.D. 15.1; $t = 2.921$ on 23 degrees of freedom, $0.01 > P > 0.001$. The diastolic pressure

Highest Blood Pressure Recorded in Each Interval

| Weeks Gestation | Number of Subjects | Mean Systolic Pressure | S.D. | S.E. | Mean Diastolic Pressure | S.D. | S.E. |
|---|---|---|---|---|---|---|---|
| NORMOTENSIVE GROUP | | | | | | | |
| 8 - 11 | 23 | 118.7 | 10.92 | 2.28 | 66.5 | 5.40 | 1.13 |
| 12 - 15 | 26 | 118.8 | 9.18 | 1.80 | 66.8 | 5.95 | 1.17 |
| 16 - 19 | 24 | 118.8 | 9.75 | 2.07 | 67.1 | 6.34 | 1.27 |
| 20 - 23 | 26 | 119.0 | 10.96 | 2.15 | 66.2 | 5.77 | 1.13 |
| 24 - 27 | 26 | 120.5 | 13.04 | 2.56 | 67.6 | 6.34 | 1.24 |
| 28 - 31 | 26 | 121.4 | 10.93 | 2.14 | 69.2 | 4.84 | 0.95 |
| 32 - 35 | 26 | 121.3 | 9.12 | 1.79 | 72.1 | 7.64 | 1.50 |
| 36 - 39 | 25 | 124.6 | 11.59 | 2.32 | 74.5 | 7.47 | 1.49 |
| 40 & over | 11 | 120.9 | 5.39 | 1.62 | 71.3 | 8.58 | 2.59 |
| (corrected) | | 123.0 | | | 71.0 | | |
| Labour | 26 | 126.9 | 11.48 | 2.25 | 82.0 | 12.38 | 2.43 |
| Hospital stay | 26 | 128.6 | 7.94 | 1.56 | 81.9 | 5.49 | 1.08 |
| 6 weeks | 26 | 121.7 | 13.03 | 2.56 | 72.0 | 8.39 | 1.65 |
| 12 weeks | 24 | 117.7 | 12.68 | 2.59 | 70.5 | 8.59 | 1.75 |
| 9 months | 15 | 117.7 | 13.74 | 3.55 | 66.3 | 9.35 | 2.41 |
| (corrected) | | 113.4 | | | 65.3 | | |
| HYPERTENSION I GROUP | | | | | | | |
| 8 - 11 | 22 | 131.1 | 13.09 | 2.79 | 75.7 | 7.23 | 1.54 |
| 12 - 15 | 23 | 129.6 | 8.52 | 1.78 | 75.9 | 6.85 | 1.43 |
| 16 - 19 | 24 | 129.6 | 9.66 | 1.97 | 77.6 | 6.78 | 1.38 |
| 20 - 23 | 24 | 127.8 | 14.13 | 2.88 | 74.2 | 7.85 | 1.60 |
| 24 - 27 | 24 | 129.4 | 12.51 | 2.55 | 75.6 | 7.81 | 1.59 |
| 28 - 31 | 24 | 132.6 | 12.88 | 2.63 | 78.5 | 8.53 | 1.74 |
| 32 - 35 | 24 | 133.9 | 13.95 | 2.85 | 83.5 | 8.11 | 1.66 |
| 36 - 39 | 24 | 139.6 | 14.73 | 3.01 | 87.6 | 11.59 | 2.37 |
| 40 & over | 12 | 140.4 | 9.16 | 2.64 | 88.6 | 10.07 | 2.91 |
| (corrected) | | 144.5 | | | 91.5 | | |
| Labour | 24 | 138.1 | 20.58 | 4.20 | 89.3 | 12.45 | 2.54 |
| Hospital Stay | 24 | 133.3 | 19.28 | 3.94 | 85.2 | 13.51 | 2.76 |
| 6 weeks | 23 | 128.4 | 14.49 | 3.02 | 80.4 | 10.68 | 2.23 |
| 12 weeks | 18 | 129.1 | 13.91 | 3.28 | 76.6 | 8.18 | 1.93 |
| 9 months | 10 | 127.0 | 11.60 | 3.67 | 77.6 | 5.56 | 1.76 |
| (corrected) | | 129.0 | | | 77.1 | | |

Table 12

Hypertension II Group

Highest Blood Pressure Recorded in Each Interval

| Weeks Gestation | Number of Subjects | Mean Systolic Pressure | S.D. | S.E. | Mean Diastolic Pressure | S.D. | S.E. |
|---|---|---|---|---|---|---|---|
| 8 - 11 | 31 | 119.3 | 12.95 | 2.33 | 66.8 | 6.54 | 1.17 |
| 12 - 15 | 33 | 120.9 | 11.16 | 1.94 | 66.4 | 7.20 | 1.25 |
| 16 - 19 | 33 | 123.6 | 10.95 | 1.91 | 67.3 | 5.77 | 0.99 |
| 20 - 23 | 36 | 121.7 | 11.99 | 2.00 | 69.4 | 6.79 | 1.15 |
| 24 - 27 | 35 | 127.9 | 8.26 | 1.40 | 68.8 | 14.21 | 2.40 |
| 28 - 31 | 36 | 129.1 | 10.49 | 1.75 | 74.4 | 8.34 | 1.39 |
| 32 - 35 | 36 | 130.7 | 12.92 | 2.15 | 81.6 | 10.05 | 1.68 |
| 36 - 39 | 36 | 136.6 | 14.71 | 2.45 | 88.1 | 11.35 | 1.89 |
| 40 & over | 23 | 134.9 | 12.38 | 2.58 | 84.4 | 8.26 | 1.72 |
| (corrected) | | 138.0 | | | 88.6 | | |
| Labour | 36 | 135.0 | 13.40 | 2.23 | 88.2 | 9.77 | 1.63 |
| Hospital stay | 36 | 130.7 | 11.36 | 1.89 | 85.4 | 9.05 | 1.51 |
| 6 weeks | 33 | 125.3 | 9.81 | 1.71 | 75.6 | 7.52 | 1.31 |
| 12 weeks | 27 | 128.7 | 13.56 | 2.61 | 74.6 | 8.75 | 1.68 |
| 9 months | 14 | 120.4 | 7.46 | 1.89 | 70.2 | 9.01 | 2.33 |
| (corrected) | | 122.4 | | | 69.9 | | |

Table 12, cont.

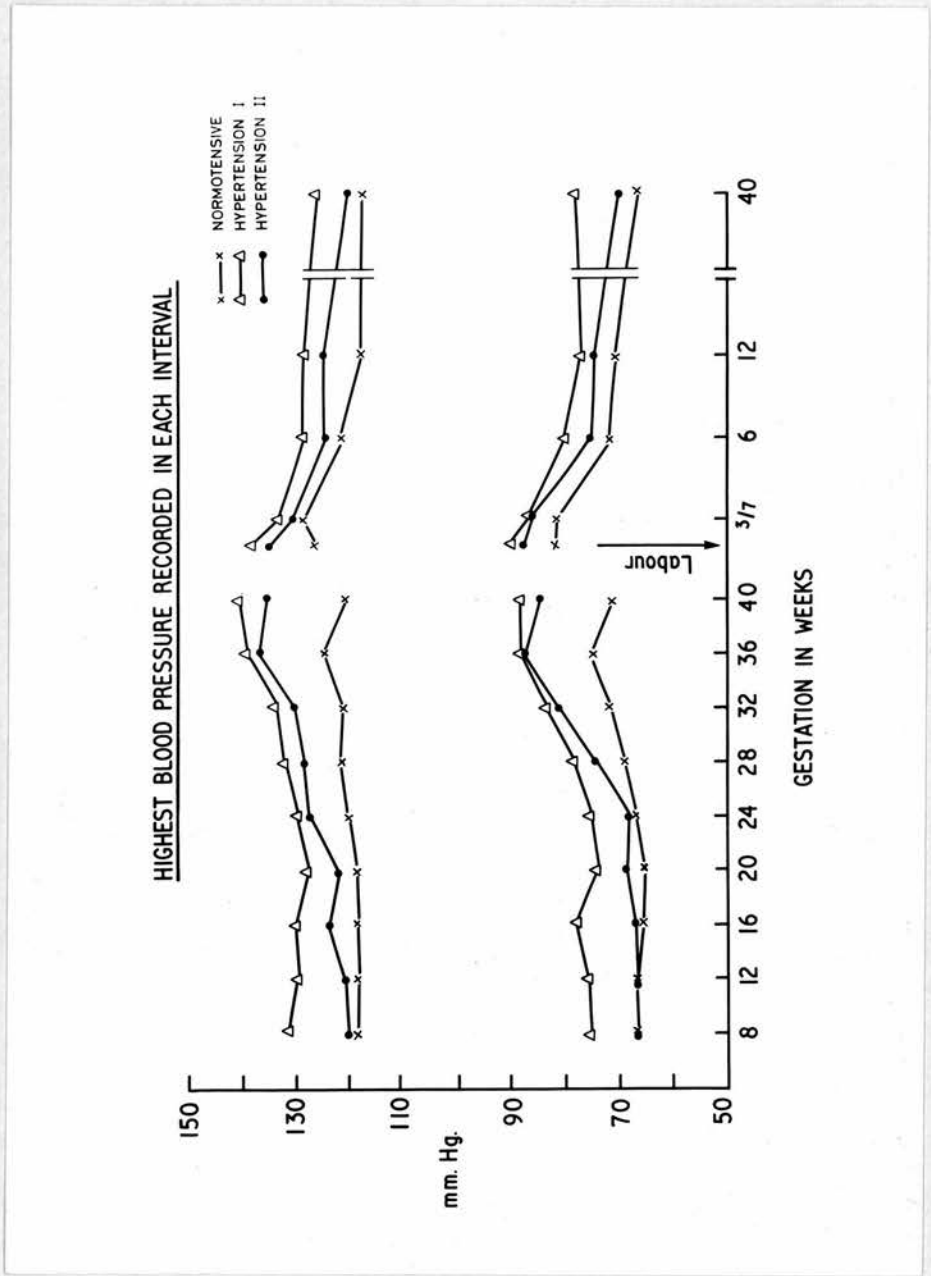



Figure IX

Highest Blood Pressure recorded in each interval.

rose by a mean of 11.5 mm. Hg. ± S.D. 14.2; t = 3.972 on 23 degrees of freedom, $P < 0.001$. There was a further rise in diastolic level during labour. During the first week of the puerperium the systolic pressure fell to first visit range; t = 0.577 on 23 degrees of freedom, $0.7 > P > 0.6$; but, the diastolic pressure remained significantly elevated; t = 3.119 on 23 degrees of freedom, $0.01 > P > 0.001$. By twelve weeks after delivery the diastolic level had fallen to that of the first visit.

This degree of change in blood pressure during pregnancy did not occur in the blood pressures recorded at the time of measurement of fore-arm flow rates.

The Hypertension II Group

There was a significant rise in both systolic and diastolic pressures from the first visit to 36 - 39 weeks gestation. The systolic pressure rose by a mean of 16.2 mm.Hg. ± S.D. 17.1; t = 5.693 on 35 degrees of freedom, $P < 0.001$. The diastolic pressure rose by a mean of 19.8 mm. Hg., ± S.D. 12.1; t = 9.824 on 35 degrees of freedom, $P < 0.001$.

The blood pressure did not change during labour and remained elevated during the first week of the puerperium. The systolic pressure in the first week of the puerperium was 10.4 mm. Hg. ± S.D. 15.1 higher than the first visit levels on average; t = 4.120 on 35 degrees of freedom, $P < 0.001$; and the diastolic pressure was 17.2 mm. Hg. ± S.D. 10.4 higher than the first visit levels on average; t = 9.920 on 35 degrees of freedom, $P < 0.001$.

Thereafter, the blood pressure fell gradually but did not reach the first visit range until 40 weeks after delivery when there was

no difference between the systolic pressures and a mean difference of only + 2.5 mm. Hg. ± S.D. 6.6 in diastolic pressure; $t = 1.447$ on 14 degrees of freedom, $0.2 > P > 0.1$.

The change in highest blood pressure recorded during pregnancy was greater than that occurring in the pressures recorded at the time of measurment of fore-arm flow rates.

Comparison of Highest Blood Pressures Recorded Between the Experimental Groups

There was no significant difference between the change in diastolic pressure during pregnancy which occurred in the normotensive and hypertension I groups; $t = 0.993$ on 47 degrees of freedom, $0.4 > P > 0.3$.

There was a highly significant difference in the increase in diastolic between the normotensive group and the hypertension II group; $t = 3.973$ on 57 degrees of freedom, $P < 0.001$, and a significant difference between the two hypertensive groups; $t = 2.368$ on 56 degrees of freedom, $0.05 > P > 0.02$.

The blood pressures at first visit were the same as those for the blood pressures taken at the time of flow measurement, the normotensive group and the hypertension II group not being significantly different from each other but both significantly lower than the hypertension I group. Similarly, a significant difference appeared between the normotensive and hypertension II group in the systolic pressure first, at 16 - 19 weeks gestation in the diastolic level later, at 28 - 31 weeks gestation.

Comparison Between the Blood Pressure at the time of Flow Measurement and Highest Blood Pressure Recorded in Each Interval

During pregnancy the blood pressure taken at the time of flow measurement showed a significant change only in the hypertension II group but when the highest blood pressures recorded in each interval were inspected there was a significant increase during pregnancy in all three experimental groups, there being the least increase in the normotensive group and the greatest increase in the hypertension II group.

Summary of Behaviour of Blood Pressure during Pregnancy

In all pregnant groups there was a significant rise in systolic and diastolic pressures during pregnancy. The diastolic pressure increased the most resulting in a relative decrease in pulse pressure towards term.

Throughout pregnancy the mean blood pressures of the hypertension I group remained significantly higher than the normotensive group and although they increased more than the normotensive group the effect was not significantly different between the two groups. The mean blood pressure of the hypertension II group was not significantly different from the normotensive group at first visit but by 16 - 19 weeks gestation the systolic level was higher than the normotensive group and by 24 - 25 and 28 - 31 weeks gestation the diastolic level was significantly higher than the normotensive group.

During the first week of the puerperium the blood pressure of all groups was significantly higher than the first visit level. The normotensive and hypertensive I groups reached first visit levels by 12 weeks after delivery but the hypertension II group did not reach first visit levels until 40 weeks after delivery.

It is important to note that when blood pressure was measured at the time of flow reading sessions no change occurred during pregnancy in the normotensive and hypertension I groups but only in the hypertension II group. Many subjects were not studied at the time of maximal blood pressure to avoid treatment effects invalidating the measurement.

## Fore-Arm Peripheral Resistance Units

Peripheral resistance units were calculated from the formula of Green et al (1944),

## The Control Group

The mean peripheral resistance unit for each subject was calculated to gave a mean reading for the 32 non-pregnant control subjects of 28.5 ± S.D. 12.2

## Relationship with Blood Pressure

The mean peripheral resistance unit for twenty-two normotensive subjects was 27.2 ± S.D. 11.5 and that for the ten hypertensive subjects was 31.4 ± S.D. 13.9. There was no significant difference between the two groups; $t = 0.891$ on 30 degrees of freedom, $0.4 > P > 0.3$

## Reproducibility Between Intervals

In seven normotensive subjects readings were obtained in each of six intervals. There was no significant decrease from first to sixth intervals; the mean decrease being 6.7 units ± S.D.30.0 $t = 0.590$ on 6 degrees of freedom, $0.6 > P > 0.5$

In five hypetensive subjects readings were obtained in each of six intervals. There was a non-significant decrease of 4.5 units ± S.D. 23.0 from first to sixth interval; $t = 0.439$ on 4 degrees of freedom $0.7 > P > 0.6$.

Table 13

| Subjects | Intervals | | | | | | Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | | 1 | 2 | 3 | 4 | 5 | 6 |
| | NORMOTENSIVE | | | | | | | HYPERTENSIVE | | | | | |
| No.1 | 23.9 | 12.4 | 8.1 | 20.8 | 16.3 | 9.5 | No.1 | 19.4 | 18.3 | 13.9 | 14.8 | 13.4 | 21.5 |
| No.2 | 34.0 | 53.7 | 61.9 | 42.9 | 50.0 | 55.6 | No.2 | 25.7 | 25.8 | 22.8 | 31.3 | 49.0 | 36.3 |
| No.3 | 14.1 | 18.1 | 19.1 | 21.1 | 35.8 | 28.6 | No.3 | 12.7 | 18.6 | 11.7 | 16.4 | 33.3 | 33.3 |
| No.4 | 77.8 | 54.2 | 70.8 | 47.9 | 30.8 | 13.2 | No.4 | 51.7 | 116.7 | 34.7 | 39.1 | 20.1 | 16.2 |
| No.5 | 38.5 | 26.9 | 30.9 | 21.5 | 26.4 | 56.4 | No.5 | 35.1 | 20.2 | 26.3 | 40.3 | 36.2 | 14.7 |
| No.6 | 37.9 | 26.9 | 13.5 | 31.4 | 15.7 | 19.7 | | | | | | | |
| No.7 | 19.3 | 36.1 | 26.5 | 28.1 | 18.3 | 15.6 | | | | | | | |
| Mean | 35.1 | 32.6 | 33.0 | 30.5 | 27.6 | 28.4 | | 28.9 | 39.9 | 21.9 | 28.4 | 30.4 | 24.4 |
| S.D. | 21.1 | 16.4 | 24.2 | 11.00 | 12.5 | 19.8 | | 15.2 | 43.0 | 9.4 | 12.2 | 14.0 | 9.9 |

Fore-Arm Peripheral Resistance Units

Control Group; Reproducibility Between Intervals

The Normotensive Group

The peripheral resistance units fell from first visit to 32 - 35 weeks gestation by a mean of 9.6 units ± S.D. 23.1. This was a significant fall; t = 2.115 on 25 degrees of freedom, $0.05 > P > 0.02$. There was no significant change following delivery; t = 0.116 on 23 degrees of freedom, $P > 0.9$. At forty weeks after delivery the mean was 27.6 units ± S.D. 17.8 which was not significantly lower than the first visit mean; t = 1.907 on 14 degrees of freedom, $0.1 > P > 0.05$.

Comparison with the Control Group

At 8 - 11 weeks gestation the mean peripheral resistance unit wa was significantly higher than the non-pregnant level; t = 2.813 on 52 degrees of freedom, $0.01 > P > 0.001$. During pregnancy there was a gradual fall towards non-pregnant levels. On the 3rd day after delivery and at forty weeks after delivery the values closely approximated the non-pregnant levels.

The Hypertension I Group

There was a mean fall in peripheral resistance units from 12 - 15 weeks to 24 - 27 weeks gestation of 9.7 units ± S.D. 20.2 which was significant; t = 2.149 on 19 degrees of freedom, $0.05 > P > 0.02$. The mean fall of 8.3 units ± S.D. 23.1 from first visit to 36 - 39 weeks gestation was just not significant; t = 1.728 on 22 degrees of freedom, $0.1 > P > 0.05$.

At forty weeks after delivery there was a mean decrease from first visit levels of 11.3 units ± S.D. 16.4 which was not significant; t = 2.181 on 9 degrees of freedom, $0.1 > P > 0.05$.

Table 14

Peripheral Resistance Units

| Weeks Gestation | NORMOTENSIVE | | | | HYPERTENSION I | | | | HYPERTENSION II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Number of Subjects | Mean | S.D. | S.E. | Number of Subjects | Mean | S.D. | S.E. | Number of Subjects | Mean | S.D. | S.E. |
| 8 - 11 | 22 | 38.6 | 14.0 | 3.0 | 21 | 35.5 | 15.7 | 3.4 | 30 | 30.2 | 12.6 | 2.3 |
| 12 - 15 | 26 | 36.5 | 20.0 | 3.9 | 21 | 38.6 | 22.1 | 4.8 | 32 | 33.5 | 15.9 | 2.8 |
| 16 - 19 | 25 | 41.0 | 21.9 | 4.4 | 24 | 37.7 | 22.0 | 4.5 | 34 | 29.2 | 20.0 | 3.4 |
| 20 - 23 | 25 | 39.1 | 21.5 | 4.3 | 22 | 34.9 | 19.6 | 4.2 | 35 | 31.7 | 17.8 | 3.0 |
| 24 - 27 | 26 | 32.5 | 14.8 | 2.9 | 23 | 29.9 | 15.0 | 3.1 | 34 | 27.5 | 16.4 | 2.8 |
| 28 - 31 | 25 | 32.8 | 18.6 | 3.7 | 22 | 33.1 | 21.2 | 4.5 | 35 | 34.6 | 26.8 | 4.5 |
| 32 - 35 | 26 | 31.6 | 17.1 | 3.4 | 24 | 31.1 | 21.1 | 4.3 | 35 | 28.7 | 20.8 | 3.5 |
| 36 - 39 | 21 | 35.1 | 18.9 | 4.1 | 24 | 28.5 | 19.1 | 3.9 | 33 | 26.7 | 22.6 | 3.9 |
| 40 & over | 9 | 26.0 | 11.9 | 4.0 | 4 | 31.8 | 19.9 | 9.9 | 16 | 21.9 | 11.5 | 3.0 |
| (corrected) | | 27.5 | | | | 32.5 | | | | 18.9 | | |
| Post-Delivery | | | | | | | | | | | | |
| 3rd day | 24 | 26.5 | 14.4 | 2.9 | 24 | 30.0 | 23.4 | 4.8 | 35 | 21.9 | 10.3 | 1.8 |
| 6 weeks | 26 | 33.4 | 13.7 | 2.7 | 23 | 39.1 | 26.8 | 5.6 | 33 | 29.5 | 16.0 | 2.8 |
| 12 weeks | 24 | 25.8 | 17.6 | 3.6 | 18 | 37.6 | 17.0 | 4.0 | 27 | 29.4 | 18.8 | 3.6 |
| 9 months | 15 | 27.6 | 17.8 | 4.6 | 10 | 24.9 | 8.7 | 2.8 | 14 | 26.1 | 14.7 | 3.9 |
| (corrected) | | 27.7 | | | | 19.8 | | | | 25.0 | | |

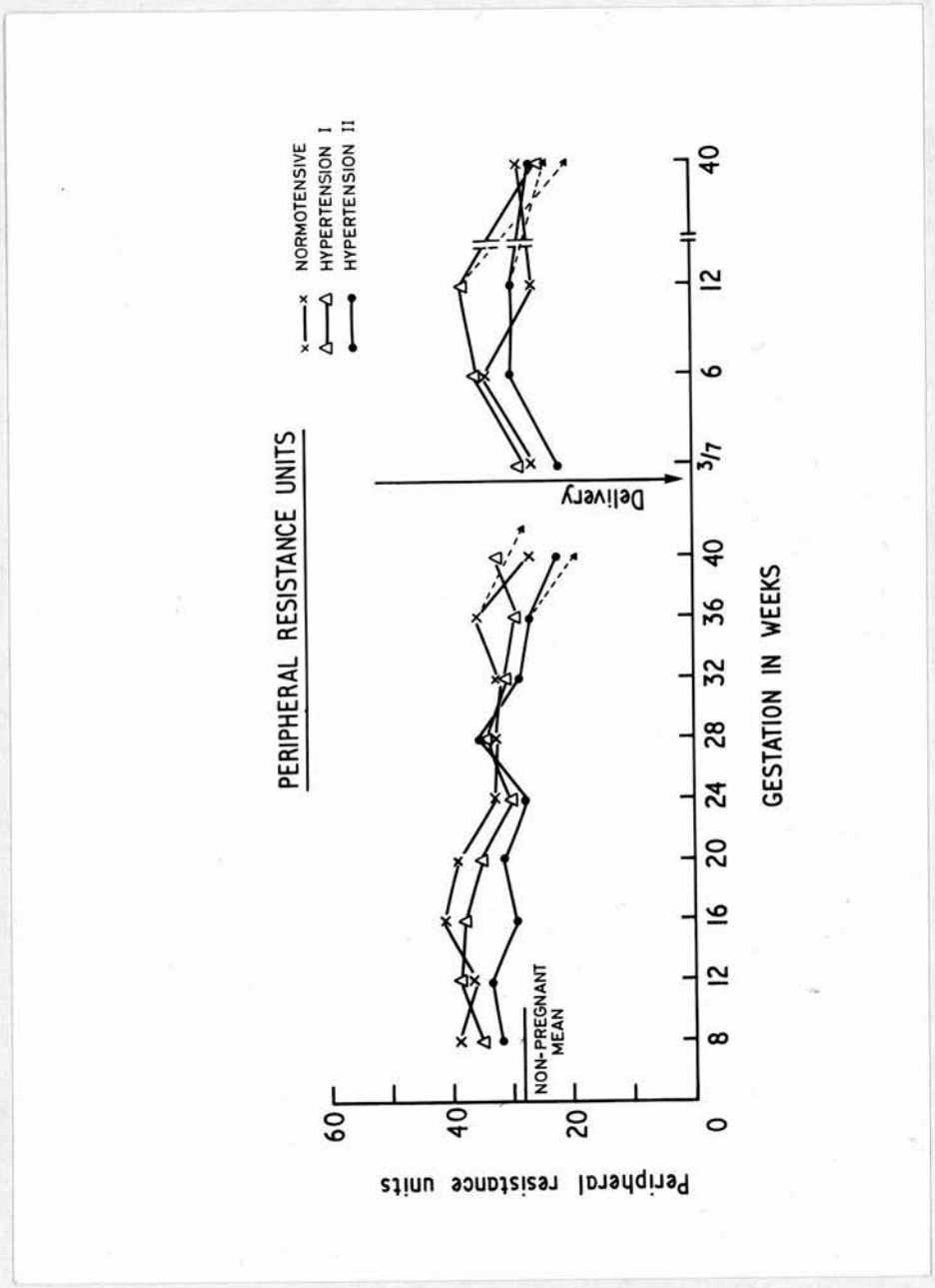



Figure XX

Fore-arm peripheral resistance units in pregnancy. The corrected figures are represented by the broken line and closed triangle.

Comparison with the Control Group

At 8 - 11 weeks gestation there was no difference from the control group; t = 1.826 on 51 degrees of freedom, $0.1 > P > 0.05$. At 12 - 15 weeks gestation it was significantly higher than the non-pregnant level; t = 2.145 on 51 degrees of freedom, $0.05 > P > 0.02$, but this was the only occasion on which a significant difference apperred. After delivery the levels approximated the non-pregnant reading.

The Hypertension II Group

No significant change occurred durigg pregnancy or the puerperium. The mean fall from 8 - 11 weeks to 24 - 27 weeks gestation was 2.1 units $\pm$ S.D. 14.7; t = 0.782 on 30 degrees of freedom, $0.5 > P > 0.4$.

At 40 weeks after delivery the level was 5.1 units $\pm$ S.D. 15.7 lower on average than the first visit level but this was not significant; t = 1.208 on 13 degrees of freedom, $0.3 > P > 0.2$.

Comparison with the Control Group

There was no significant difference from the control group; e.g. comparing 12 - 15 weeks gestation with the non-pregnant level gave t = 1.411 on 62 degrees of freedom, $0.2 > P > 0.1$.

Comparison between the Blood Pressure Groups

The mean peripheral resistance units of the normotensive group were higher than those of the hypertension II group throughout pregnancy except at 28 - 31 weeks gestation. The difference was significant at 16 - 19 weeks gestation; t = 2.152 on 57 degrees of freedom, $0.05 > P > 0.02$ but not any any other time, e.g. at 36 weeks t = 1.417.on 52 degrees of freedom, $0.2 > P > 0.1$.

The normotensive group peripheral resistance units were very little higher than those of the hypertension I group during pregnancy.

By forty weeks after delivery the mean units for each group closely approximated each other.

## SUMMARY

The peripheral resistance units fell during pregnancy but significant effects were seen only in the normotensive group and transiently in the hypertension I group. On the whole the peripheral resistance units of the normotensive group were higher than the hypertension I group which were higher than the hypertension II group during pregnancy but these differences were not significant except for one occasion at 16 - 19 weeks gestation when the normotensive group was significantly greater than the hypertension II group.

Compared with the control group both normotensive and hypertension I groups were significantly higher in early pregnancy but thereafter did not differ.

At 40 weeks after delivery all the experimental groups and non-pregnant control group gave almost identical mean values.

## PULSE RATE

### Control Group

The mean pulse rate per minute for the control group was calculated from the mean pulse rate for each of the 32 subjects and was 72.4 beats per minute ± S.D. 10.21.

Blood Pressure Effect

The mean pulse rate for the normotensive group was 70.6 beats per minute ± S.D. 9.3 and that forthe hypertensive group was 76.4 beats per minute ± S.D. 11.6. There was no significant difference between the two groups; $t = 1.521$ on 30 degrees of freedom, $0.2 > P > 0.1$.

Reproducibility

Fourteen subjects who were examined in each of six intervals showed a mean decrease in pulse rate from the first to sixth interval of 5.4 beats per minute. This was not significant; $t = 1.463$ on 13 degrees of freedom, $0.2 > P > 0.1$.

### The Normotensive Group

During pregnancy there was no significant change in pulse rate. The mean increase of 7.0 beats/minute ± S.D. 15.5 was not significant; $t = 2.077$ on 20 degrees of freedom, $0.1 > P > 0.05$.

On the third day after delivery the mean pulse rate fell significantly below the pregnancy rate and remained close to this level. A t-test comparing the rate at 12 - 15 weeks gestation with the rate at 40 weeks after delivery gave $t = 3.208$ on 14 degrees of freedom, $0.01 > P > 0.001$.

## Pulse Rate

### Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No.1 | 72 | 76 | 72 | 92 | 76 | 84 |
| No.2 | 60 | 70 | 68 | 60 | 52 | 60 |
| No.3 | 86 | 80 | 76 | 88 | 72 | 72 |
| No.4 | 72 | 68 | 72 | 72 | 72 | 64 |
| No.5 | 72 | 74 | 64 | 68 | 60 | 50 |
| No.6 | 60 | 60 | 60 | 56 | 72 | 68 |
| No.7 | 80 | 68 | 72 | 70 | 72 | 72 |
| No.8 | 64 | 78 | 72 | 64 | 68 | 60 |
| No.9 | 96 | 95 | 100 | 72 | 84 | 72 |
| No.10 | 92 | 78 | 74 | 60 | 84 | 88 |
| No.11 | 60 | 78 | 76 | 72 | 84 | 84 |
| No.12 | 72 | 72 | 68 | 72 | 72 | 60 |
| No.13 | 96 | 64 | 64 | 72 | 72 | 96 |
| No.14 | 72 | 60 | 50 | 56 | 60 | 48 |
| Mean | 75.3 | 72.9 | 70.6 | 69.6 | 71.4 | 69.9 |
| S.D. | 12.9 | 9.2 | 11.0 | 10.6 | 9.4 | 14.2 |

Table 15

Table 16

Pulse Rate

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Number of Subjects | Mean Pulse Rate | S.D. | S.E. | Number of Subjects | Mean Pulse Rate | S.D. | S.E. | Number of Subjects | Mean Pulse Rate | S.D. | S.E. |
| 8 - 11 | 17 | 82.9 | 15.31 | 3.71 | 15 | 87.2 | 16.33 | 4.22 | 19 | 83.8 | 11.13 | 2.55 |
| 12 - 15 | 21 | 81.5 | 13.10 | 2.86 | 19 | 90.9 | 11.04 | 2.53 | 23 | 86.3 | 12.39 | 2.58 |
| 16 - 19 | 21 | 81.5 | 9.31 | 2.03 | 22 | 92.5 | 16.00 | 3.41 | 25 | 88.7 | 10.11 | 2.02 |
| 20 - 23 | 21 | 84.5 | 9.91 | 2.16 | 21 | 89.1 | 11.89 | 2.59 | 27 | 87.3 | 11.26 | 2.17 |
| 24 - 27 | 21 | 84.8 | 9.91 | 2.16 | 20 | 87.4 | 13.11 | 2.93 | 26 | 90.6 | 9.42 | 1.85 |
| 28 - 31 | 21 | 88.5 | 13.11 | 2.86 | 21 | 88.5 | 14.68 | 3.20 | 28 | 88.6 | 12.71 | 2.40 |
| 32 - 35 | 21 | 87.5 | 12.63 | 2.76 | 21 | 90.2 | 14.94 | 3.26 | 28 | 89.6 | 15.35 | 2.90 |
| 36 - 39 | 17 | 87.3 | 14.93 | 3.62 | 22 | 87.0 | 12.37 | 2.64 | 28 | 87.7 | 11.41 | 2.16 |
| 40 & over | 7 | 86.6 | 14.27 | 5.39 | 10 | 83.3 | 11.24 | 3.55 | 17 | 86.9 | 10.82 | 2.62 |
| (corrected) | | 86.6 | | | | 80.2 | | | | 85.6 | | |
| Post-Delivery | | | | | | | | | | | | |
| 3rd day | 26 | 74.7 | 10.83 | 2.12 | 24 | 82.3 | 14.56 | 2.97 | 35 | 81.9 | 7.64 | 1.29 |
| 6 weeks | 21 | 73.0 | 12.31 | 2.69 | 20 | 78.7 | 12.59 | 2.82 | 25 | 79.7 | 13.61 | 2.72 |
| 12 weeks | 19 | 79.2 | 15.07 | 3.46 | 16 | 78.8 | 9.00 | 2.25 | 22 | 83.0 | 9.95 | 2.12 |
| 9 months | 15 | 74.3 | 10.55 | 2.72 | 10 | 85.4 | 13.70 | 4.33 | 14 | 85.1 | 15.41 | 4.12 |
| (corrected) | | 78.3 | | | | 83.4 | | | | 85.7 | | |

Comparison with the Non-Pregnant Control Group

The pulse rate of the normotensive group during pregnancy was significantly higher than that of the control group. For example, at 8 - 11 weeks gestation $t = 2.870$ on 47 degrees of freedom, $0.01 > P > 0.001$. After delivery the pulse rate approximated that of the control group.

Reproducibility in the First Two Intervals

There was no difference in rate throughout pregnancy.

The Hypertension I Group

No significant change occurred during pregnancy or the post-natal period. The mean increase from 8 - 11 weeks gestation to 16 - 19 weeks gestation was 7.1 beats/minute $\pm$ S.D. 14.3; $t = 1.915$ on 14 degrees of freedom, $0.1 > P > 0.05$.

Comparison with the Control Group

The mean pulse rate was not different from the normotensive group at 8 - 11 weeks gestation which was significantly higher than the non-pregnant control group.

For a comparison at 9 months after delivery see Hypertension II.

Reproducibility in the First Two Intervals

There was no change throughout pregnancy.

The Hypertension II Group

No significant change occurred during pregnancy and the puerperium. A paired t-test between values at 8 - 11 weeks and 24 - 27 weeks gestation gave a mean increase of 4.9 beats per minute $\pm$ S.D. 13.0; $t = 1.591$ on 17 degrees of freedom, $0.2 > P > 0.1$.

Comparison with the Control Group

At 8 - 11 weeks gestation the pulse rate approximated that of the normotensive group which was significantly higher than the non-pregnant group.

At 40weeks after delivery the mean pulse rate of both hypertensive groups was significantly higher than the non-pregnant normotensive control group; $t = 4.064$ on 44 degrees of freedom, $P < 0.001$ but not significantly higher than the hypertensive non-pregnant control group; $t = 1.721$ on 32 degrees of freedom, $0.1 > P > 0.05$.

Reproducibility Between the First Two Intervals

No change occurred throughout pregnancy.

Relationship Between the Experimental Groups

At 8 - 11 weeks gestation the normotensive group pulse rate approximated that of the hypertension II group and there was no significant difference between the normotensive and hypertension I group; $t = 0.755$ on 30 degrees of freedom, $0.5 > P > 0.4$.

By 16 - 19 weeks gestation there was a significant difference between the normotensive group and the hypertensive groups which had faster pulse rates. Normotensive group compared with hypertensive I group gave $t = 2.738$ on 41 degrees of freedom, $0.1 > P > 0.001$ and compared with hypertension II group gave $t = 2.493$ on 44 degrees of freedom, $0.01 > P > 0.001$. The difference decreased with advancing pregnancy and disappeared by 28 - 31 weeks gestation.

A significant decrease in pulse rate occurred in the normotensive group by 3 days after delivery. The hypertensive groups remained unchanged. The normotensive rate compared with the combined

hypertensive rates gave t = 2.954 on 83 degrees of freedom, $0.01 > P > 0.001$. This difference was sustained after delivery and included the nine-month post-delivery interval.

Summary of Pulse Rate Changes During Pregnancy

During pregnancy there is little change in pulse rate in any group. All three groups remain significantly higher than the non-pregnant control group and did not differ from each other except at 12 - 15 weeks and 16 - 19 weeks gestation when a significantly higher rate wasfound in the hypertensive groups.

After delivery the pulse rate in the normotensive group fell to the control group level by 3 days and remained at this level. In the hypertensive groups the pulse rate remained at the antenatal level and was significantly higher than the non-pregnant normotensive pulse rate but not significantly different from the hypertensive non-pregnant level.

Other Changes in Pregnancy

## ORAL TEMPERATURE

### The Control Group

The mean body temperature of the 32 non-pregnant subjects was $97.8^{\circ}$ F $\pm$ S.D. 0.60.

### The Effect of Blood Pressure

The mean oral temperature of the 22 normotensive subjects was $97.8^{\circ}$ F $\pm$ S.D. 0.6 and that for the hypertensive group was $98.0^{\circ}$ F $\pm$ S.D. 0.7, which were not significantly different; $t = 1.223$ on 30 degrees of freedom, $0.3 > P > 0.2$.

### Reproducibility Between Intervals

In 14 subjects readings were obtained in each of six intervals. There was no significant difference between the first and last interval; $t = 0.580$ on 13 degrees of freedom, $0.6 > P > 0.5$.

### The Effect of the Menstrual Cycle

In 19 subjects temperatures were available for pre- and post-ovulatory phases of the cycle. There was a mean increase of $0.06^{\circ}$ F in the second half of the cycle, which was not significant; $t = 0.548$ on 18 degrees of freedom, $0.6 > P > 0.5$.

### The Pregnant Groups

The oral temperatures were very similar throughout pregnancy in the three blood pressure groups.

There was a significant decrease in oral temperature from first visit to last pre-delivery visit. The normotensive group showed a mean fall of $1.05^{\circ}$ F $\pm$ S.D. 0.85; $t = 5.641$ on 20 degrees of freedom, $P < 0.001$. In the hypertension I group there was a mean fall of $0.72^{\circ}$ F $\pm$ S.D. 1.06; $t = 3.132$ on 20 degrees of freedom, $0.01 > P > 0.001$.

Oral Temperature

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 98.0 | 98.4 | 97.0 | 98.2 | 97.6 | 98.0 |
| No. 2 | 96.2 | 98.0 | 97.2 | 97.2 | 97.0 | 96.0 |
| No. 3 | 97.8 | 97.0 | 97.8 | 98.2 | 97.8 | 97.0 |
| No. 4 | 98.0 | 99.2 | 98.4 | 98.4 | 98.4 | 98.4 |
| No. 5 | 98.4 | 97.8 | 98.4 | 97.8 | 97.0 | 97.8 |
| No. 6 | 97.2 | 98.0 | 97.6 | 98.0 | 98.0 | 97.8 |
| No. 7 | 98.6 | 97.8 | 97.8 | 98.4 | 98.4 | 98.0 |
| No. 8 | 98.4 | 98.8 | 97.8 | 98.4 | 98.4 | 97.8 |
| No. 9 | 98.4 | 97.8 | 98.8 | 98.6 | 98.6 | 98.8 |
| No. 10 | 97.8 | 97.6 | 98.4 | 98.4 | 97.4 | 97.6 |
| No. 11 | 97.0 | 97.8 | 98.4 | 97.6 | 97.6 | 97.0 |
| No. 12 | 98.0 | 97.8 | 97.4 | 98.0 | 97.0 | 97.0 |
| No. 13 | 97.0 | 98.0 | 98.8 | 98.4 | 98.4 | 97.8 |
| No. 14 | 97.2 | 98.0 | 97.2 | 97.2 | 98.2 | 97.8 |
| Mean | 97.7 | 98.0 | 97.9 | 98.0 | 97.8 | 97.6 |
| S.D. | 0.70 | 0.53 | 0.61 | 0.45 | 0.58 | 0.69 |

Table 17

Body Temperature

All Pregnant Groups

| Weeks Gestation | Number of Subjects | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 49 | 98.3 | 0.65 | 0.09 |
| 12 - 15 | 64 | 98.2 | 0.63 | 0.08 |
| 16 - 19 | 67 | 98.1 | 0.57 | 0.07 |
| 20 - 23 | 68 | 98.0 | 0.58 | 0.07 |
| 24 - 27 | 67 | 98.0 | 0.68 | 0.08 |
| 28 - 31 | 69 | 97.9 | 0.73 | 0.09 |
| 32 - 35 | 71 | 97.8 | 0.64 | 0.08 |
| 36 - 39 | 68 | 97.6 | 0.73 | 0.09 |
| 40 & over | 33 | 97.7 | 0.71 | 0.12 |
| (corrected) | | 97.7 | | |
| Post-Delivery | | | | |
| 3rd day | 84 | 98.0 | 0.63 | 0.07 |
| 6 weeks | 66 | 97.7 | 0.78 | 0.10 |
| 12 weeks | 57 | 97.7 | 0.82 | 0.11 |
| 9 months | 39 | 98.0 | 0.71 | 0.11 |
| (corrected) | | 97.9 | | |

Table 18

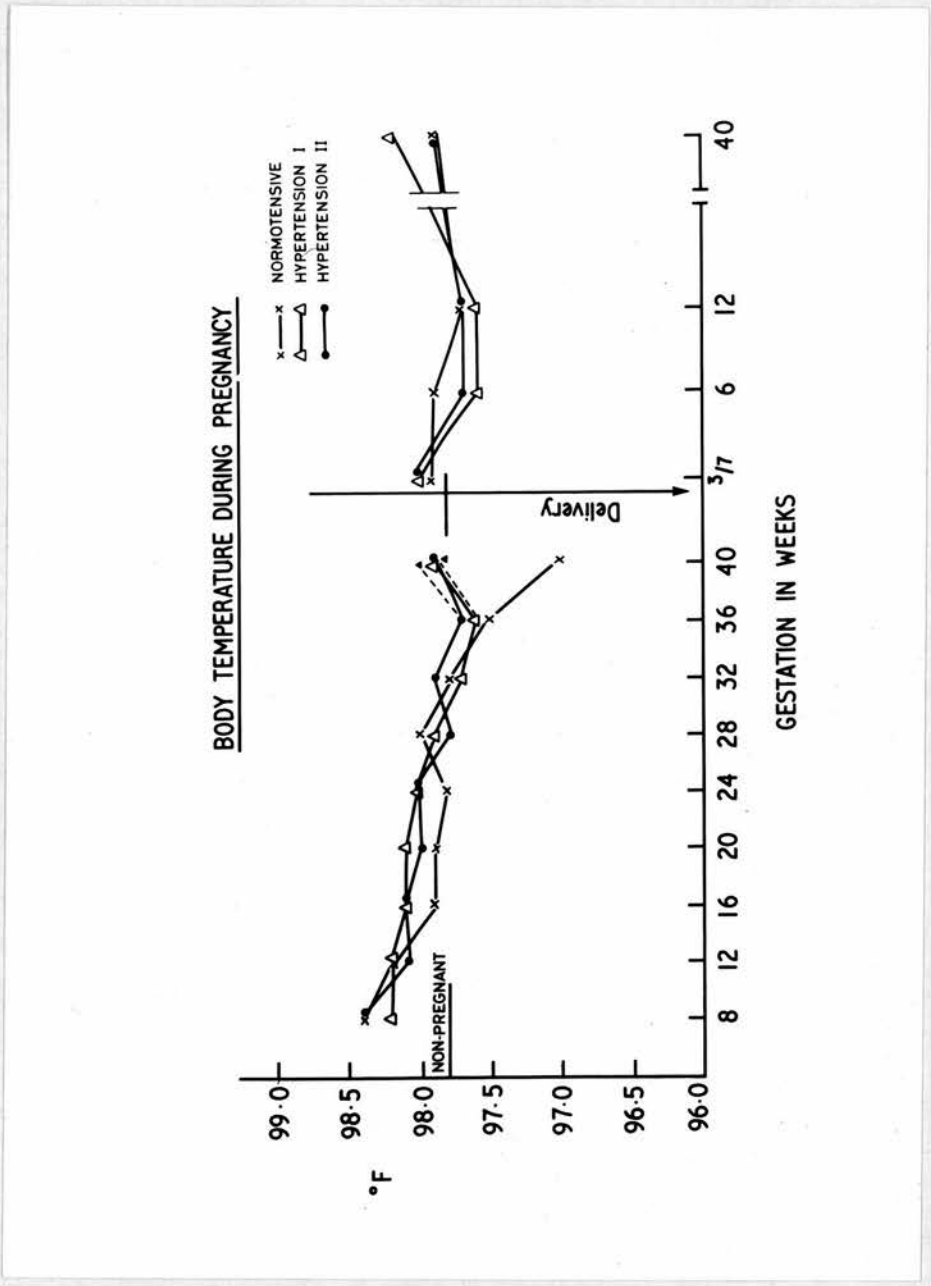



Figure XXI

Body Temperature during pregnancy. The corrected figures are represented by a broken line and closed triangle.

In the hypertension II group the fall was least, i,e. 0.61° F ± S.D. 0.76; t = 4.128 on 26 degrees of freedom, $P < 0.001$. The amount of decrease of oral temperature was not significantly different between the groups. Normotensive temperature fall compared with that of hypertension I group gave t = 1.344 on 40 degrees of freedom, $0.2 > P > 0.1$; and compared with that of hypertension II group gave t = 1.895 on 46 degrees of freedom, $0.1 > P > 0.05$. The results were therefore considered in one group for comparison with the non-pregnant control group.

## Relationship with the Control Group

The mean temperature of the pregnant groups was 0.5° F higher than the non-pregnant control group at 8 - 11 weeks gestation; a significant difference ; t = 3.463 on 79 degrees of freedom, $0.01 > P > 0.001$.

Thereafter the mean body temperature fell steadily reaching non-pregnant levels at 24 - 27 weeks and continued to fall below this level but was never significantly lower than the non-pregnant mean.

## Post-Natal Temperature

At twelve weeks after delivery the temperature was significantly lower than the 8 - 11 week reading by 0.81° F ± S.D. 1.0; t = 6.231 on 56 degrees of freedom, $P < 0.001$, but was not different from the mean of the non-pregnant group.

## SUMMARY

The oral temperature at 8 - 11 weeks gestation was significantly higher than the non-pregnant control group and fell steadily

during pregnancy to below non-pregnant levels but not significantly lower. After delivery the mean temperature was not significantly different from non-pregnant levels.

There was no significant difference between the blood pressure groups.

## FORE-ARM TEMPERATURE

### The Control Group

The mean fore-arm skin temperature of the 32 non-pregnant subjects was 33.4° C. ± S.D. 1.0 and was calculated from the mean skin temperatures for each subject.

The mean fore-arm skin temperature for the 22 non-pregnant normotensive subjects was 33.7° C. ± S.D. 0.71, which was just not significantly higher than that of the 10 hypertensive subjects which was 33.0° C. ± S.D. 1.35; $t = 1.788$ on 25 degrees of freedom, $0.1 > P > 0.05$.

Reproducibility Between Intervals

Readings were obtained in 11 subjects in each of 6 intervals. There was a mean drop in skin temperature of 0.58° C. ± S.D. 1.72 from first to sixth intervals but this was not significant; $t = 1.116$ on 10 degrees of freedom, $0.3 > P > 0.2$.

### The Pregnant Groups

There were small numbers in each group and the theory that the data did not represent a straight line was rejected on analysis; $F = 1.627$ on 6-26 degrees of freedom, $P > 0.05$. The mean temperature during pregnancy was highest in the hypertension II group, 34.25°C. ± S.D. 0.22 and lowest in the hypertension I group, 33.71°C. ± S.D. 0.28. This difference was significant; $t = 2.339$ on 21 degrees of freedom, $0.05 > P > 0.01$. The mean skin temperature during pregnancy for the normotensive group was slightly lower than the hypertension II group, being 34.02°C. ± S.D. 0.31 but was also significantly higher than the hypertension I group; $t = 2.142$ on 15 degrees of freedom, $0.05 > P > 0.01$.

Fore-Arm Skin Temperature

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 34.3 | 35.6 | 36.0 | 36.3 | 35.0 | 35.0 |
| No. 2 | 34.0 | 32.0 | 33.0 | 33.6 | 32.3 | 34.0 |
| No. 3 | 35.3 | 35.0 | 33.6 | 34.0 | 32.6 | 36.0 |
| No. 4 | 34.0 | 35.6 | 32.3 | 31.6 | 34.0 | 31.3 |
| No. 5 | 35.6 | 37.0 | 35.6 | 32.3 | 33.3 | 34.5 |
| No. 6 | 34.0 | 33.0 | 34.0 | 33.5 | 34.0 | 33.0 |
| No. 7 | 36.3 | 33.3 | 34.5 | 33.5 | 33.5 | 32.5 |
| No. 8 | 31.0 | 32.6 | 32.6 | 34.6 | 32.6 | 33.3 |
| No. 9 | 34.5 | 35.5 | 33.5 | 33.0 | 34.5 | 33.0 |
| No.10 | 33.0 | 34.3 | 33.3 | 34.3 | 34.0 | 33.8 |
| No.11 | 34.0 | 35.0 | 35.0 | 35.0 | 34.0 | 34.6 |
| Mean | 34.2 | 34.4 | 33.9 | 33.8 | 33.6 | 33.7 |
| S.D. | 1.4 | 1.5 | 1.2 | 1.3 | 0.8 | 1.3 |

Table 19

Fore-Arm Skin Temperature

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. |
| 8 - 11 | 8 | 34.2 | 1.17 | 0.41 | 7 | 33.4 | 1.79 | 0.68 | 11 | 34.3 | 1.61 | 0.49 |
| 12 - 15 | 9 | 34.4 | 1.35 | 0.45 | 7 | 33.8 | 1.57 | 0.59 | 14 | 34.4 | 1.09 | 0.29 |
| 16 - 19 | 9 | 33.7 | 0.89 | 0.30 | 9 | 34.0 | 1.15 | 0.38 | 16 | 34.0 | 0.93 | 0.23 |
| 20 - 23 | 9 | 33.6 | 1.09 | 0.36 | 9 | 33.9 | 0.91 | 0.30 | 18 | 33.8 | 0.96 | 0.23 |
| 24 - 27 | 10 | 34.3 | 1.38 | 0.44 | 8 | 33.7 | 1.17 | 0.41 | 16 | 34.6 | 1.61 | 0.40 |
| 28 - 31 | 10 | 34.6 | 1.01 | 0.32 | 8 | 33.7 | 1.09 | 0.39 | 17 | 34.1 | 1.06 | 0.26 |
| 32 - 35 | 12 | 34.3 | 1.43 | 0.41 | 9 | 33.8 | 0.94 | 0.31 | 19 | 34.4 | 1.52 | 0.35 |
| 36 - 39 | 8 | 33.6 | 1.80 | 0.64 | 9 | 33.4 | 0.82 | 0.27 | 19 | 34.2 | 1.38 | 0.32 |
| 40 & over | 3 | 33.8 | 0.76 | 0.44 | 2 | 33.5 | - | - | 10 | 34.5 | 1.45 | 0.46 |
| Post-Delivery | | | | | | | | | | | | |
| 3 days | 13 | 34.5 | 1.05 | 0.29 | 9 | 34.2 | 1.06 | 0.35 | 20 | 34.2 | 1.27 | 0.28 |
| 6 weeks | 16 | 34.1 | 0.92 | 0.23 | 8 | 33.2 | 1.19 | 0.42 | 19 | 33.9 | 1.16 | 0.27 |
| 12 weeks | 14 | 34.1 | 1.19 | 0.32 | 7 | 33.5 | 1.06 | 0.40 | 15 | 34.0 | 1.57 | 0.41 |
| 40 weeks | 12 | 34.2 | 1.36 | 0.39 | 5 | 34.5 | 0.61 | 0.27 | 10 | 34.7 | 1.24 | 0.39 |

Table 20

Comparison with the Control Groups

The normotensive pregnant group mean fore-arm skin temperature was not significantly different from the normotensive non-pregnant group; $t = 1.291$ on 29 degrees of freedom, $0.3 > P > 0.2$.

The hypertension I group during pregnancy was not significantly different from the hypertensive non-pregnant group; $t = 1.455$ on 16 degrees of freedom, $0.2 > P > 0.1$.

The hypertension II group mean fore-arm skin temperature during pregnancy was significantly higher than the normotensive non-pregnant group; $t = 2.896$ on 35 degrees of freedom, $0.01 > P > 0.001$, and also significantly higher than the hypertensive non-pregnant group; $t = 3.553$ on 23 degrees of freedom, $0.01 > P > 0.001$.

After Delivery

No significant changes occurred in the experimental groups after delivery. By 40 weeks after delivery the mean skin temperature was lowest in the normotensive group and highest in the hypertension II group but there was no significant difference between the two; $t = 0.893$ on 20 degrees of freedom, $0.4 > P > 0.3$.

## TEMPERATURE GRADIENT BETWEEN BODY (ORAL) AND FORE-ARM SKIN

### Control Group

The mean difference in temperature between oral and skin readings for 26 non-pregnant subjects was 3.11°C. ± S.D. 0.99.

### Relationship with Blood Pressure

The temperature gradient in the 17 normotensive subjects was 2.83°C. ± S.D. 0.61 which was significantly lower than that for the hypertensive group which was 3.64°C. ± S.D. 1.34; $t = 2.134$ on 24 degrees of freedom, $0.05 > P > 0.02$.

### Reproducibility Between Intervals

Readings were obtained from 9 subjects in each of 6 intervals. There was a mean increase of temperature gradient during this period of 0.68°C. ± S.D. 1.80 which was not significant; $t = 1.130$ on 8 degrees of freedom, $0.3 > P > 0.2$.

### The Pregnant Groups

There was an overall decrease in temperature gradient during pregnancy of 0.45°C. ± S.D. 1.27 from 8 - 11 weeks gestation to 32 - 35 weeks gestation; $t = 2.130$ on 35 degrees of freedom, $0.05 > P > 0.02$.

Throughout pregnancy the greatest temperature gradient was in the hypertension I group and at 8 - 11 weeks gestation it was not significantly different from the hypertensive non-pregnant group; $t = 0.416$ on 14 degrees of freedom, $0.7 > P > 0.6$. At 8 - 11 weeks gestation the normotensive and hypertension II group were not significantly different from the normotensive non-pregnant group. By 6 weeks after delivery the hypertension I group had regained the hypertensive non-pregnant mean temperature gradient and the normotensive

Oral minus Fore-Arm Skin Temperature

Control Group: Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No.1 | 1.67 | 4.67 | 3.22 | 2.62 | 3.81 | 1.56 |
| No.2 | 1.26 | 1.11 | 2.96 | 2.78 | 3.96 | 0.11 |
| No.3 | 2.37 | 1.29 | 0.11 | 0.48 | 1.44 | 1.67 |
| No.4 | 2.22 | 1.07 | 4.14 | 5.07 | 2.67 | 5.26 |
| No.5 | 1.24 | 2.69 | 1.51 | 4.37 | 3.70 | 2.61 |
| No.6 | 2.11 | 3.56 | 2.89 | 2.83 | 2.44 | 3.11 |
| No.7 | 0.37 | 3.26 | 1.83 | 3.28 | 2.61 | 3.61 |
| No.8 | 2.06 | 0.94 | 3.39 | 3.78 | 1.83 | 3.44 |
| No.9 | 5.22 | 4.67 | 4.22 | 1.62 | 4.18 | 3.26 |
| Mean | 2.20 | 2.58 | 2.70 | 2.98 | 2.96 | 2.74 |
| S.D. | 1.07 | 1.54 | 1.33 | 1.38 | 0.99 | 1.48 |

Table 21

## Temperature Gradient

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. |
| 8 - 11 | 8 | 2.93 | 0.25 | 0.09 | 7 | 3.33 | 1.65 | 0.62 | 12 | 2.60 | 1.30 | 0.04 |
| 12 - 15 | 9 | 2.45 | 1.40 | 0.47 | 7 | 2.82 | 1.47 | 0.56 | 14 | 2.31 | 1.07 | 0.29 |
| 16 - 19 | 9 | 2.83 | 0.94 | 0.31 | 8 | 2.85 | 1.06 | 0.38 | 16 | 2.73 | 0.86 | 0.21 |
| 20 - 23 | 9 | 2.92 | 1.08 | 0.36 | 8 | 2.73 | 0.92 | 0.32 | 18 | 2.92 | 0.93 | 0.22 |
| 24 - 27 | 9 | 2.41 | 1.36 | 0.45 | 8 | 3.02 | 0.85 | 0.30 | 17 | 2.08 | 1.49 | 0.36 |
| 28 - 31 | 9 | 1.90 | 0.86 | 0.29 | 8 | 2.81 | 1.02 | 0.36 | 17 | 2.40 | 1.03 | 0.25 |
| 32 - 35 | 9 | 2.30 | 1.40 | 0.47 | 8 | 2.66 | 1.02 | 0.36 | 19 | 2.15 | 1.51 | 0.35 |
| 36 - 39 | 8 | 2.61 | 1.77 | 0.62 | 8 | 3.19 | 0.90 | 0.32 | 18 | 2.05 | 1.24 | 0.29 |
| 40 & over | 3 | 2.20 | 0.54 | 0.31 | 2 | 3.17 | 0.16 | 0.11 | 8 | 1.91 | 1.33 | 0.47 |
| Post-Delivery | | | | | | | | | | | | |
| 3 days | 9 | 1.80 | 1.04 | 0.35 | 8 | 2.40 | 1.09 | 0.38 | 18 | 2.38 | 1.31 | 0.31 |
| 6 weeks | 9 | 2.47 | 0.94 | 0.31 | 7 | 3.60 | 0.86 | 0.32 | 18 | 2.57 | 1.08 | 0.26 |
| 12 weeks | 7 | 2.15 | 0.90 | 0.34 | 4 | 3.18 | 0.76 | 0.38 | 14 | 2.33 | 1.38 | 0.37 |
| 40 weeks | 5 | 2.72 | 0.88 | 0.39 | 0 | - | - | - | 8 | 2.25 | 0.97 | 0.34 |

Table 22

and hypertension II group were not significantly different from the non-pregnant normotensive group. A t-test comparing hypertension I and II groups at 6 weeks after delivery gave $t = 2.245$ on 23 degrees of freedom, $0.05 > P > 0.02$.

## BLOOD VOLUME

Blood volume was estimated by means of Evans' Blue Dye in 67 subjects on 717 occasions; between 7 and 13 occasions each. Twenty-four subjects were normotensive, 18 subjects fell into the hypertension I group and 25 subjects were included in the hypertension II group.

### Control Values

As there was no significant change in blood volume after the 3rd day following delivery, the blood volumes from 6 weeks to 40 weeks after delivery were used as control figures.

### The Relationship Between Surface Area and Blood Volume

The blood volume was related to the surface area of the subject. A regression line of last recorded post-natal blood volume on surface area was calculated and gave $b = 3.114$ with standard error of 0.845; $t = 3.686$ on 65 degrees of freedom, $P < 0.001$. The mean blood volume was 4.337 litres $\pm$ S.D. 0.761 and the mean surface area was 1.59 square metres $\pm$ S.D. 0.10.

As there was no significant difference between the surface areas for eacheexperimental group no correction was required.for surface area when comparing the blood volumes of the experimental groups.

### The Relationship Between Blood Volume and Fore-Arm Flow

The mean fore-arm flow rate during the period 6 weeks to 40 weeks after delivery was examined for a relationship with the mean blood volume for the same period. The relationship was not significant; $t = 1.672$ on 64 degrees of freedom, $0.1 > P > 0.5$.

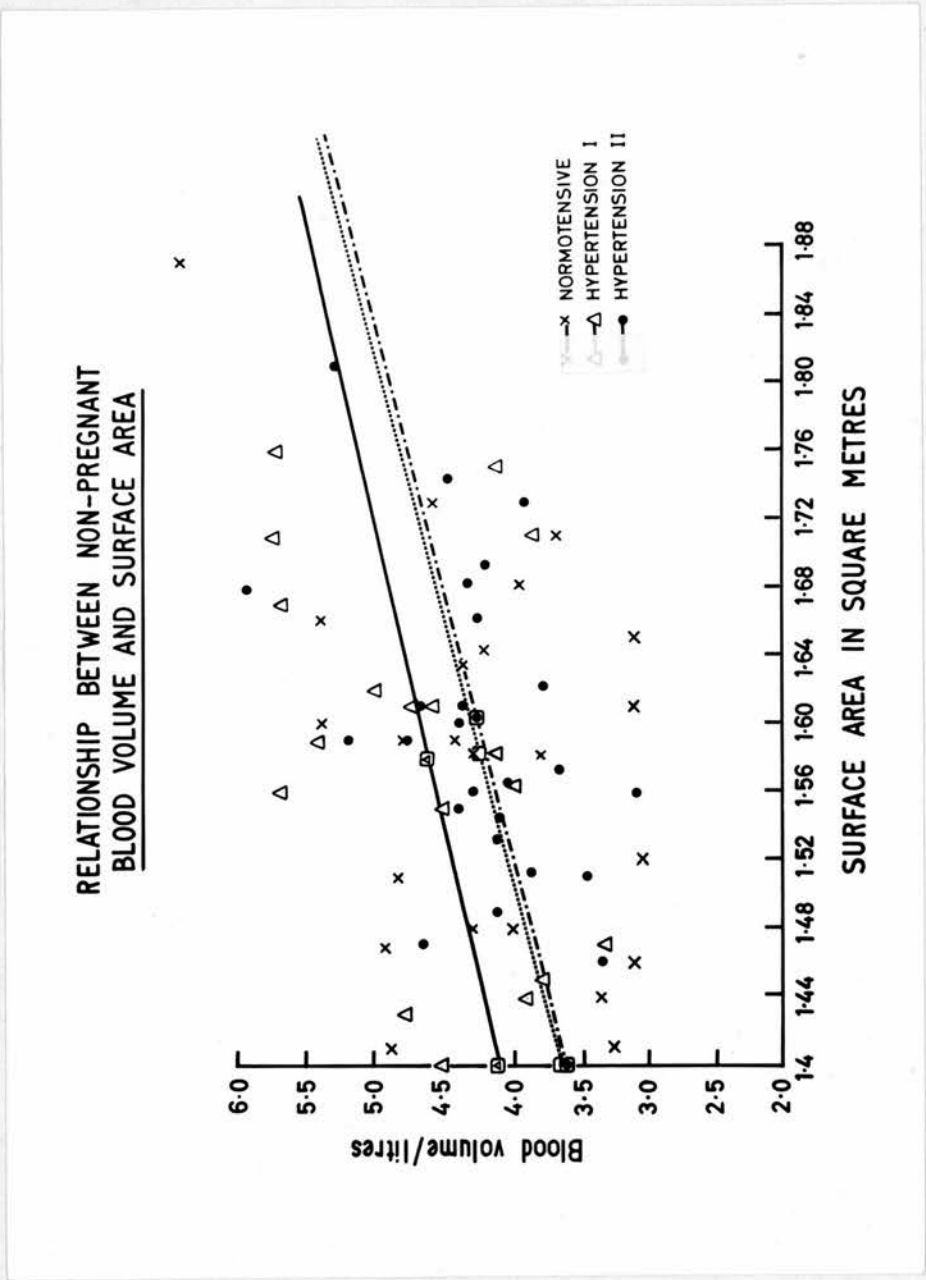



Figure XXII

Relationship between non-pregnant blood volume and surface area. The regression lines are represented by a dotted line and open squares for the patients who had a normotensive pregnancy; by a continuous line and open triangles within open squares for the Hypertension I group and an interrupted line with closed circles in open square for the Hypertension II group.

Pregnant Groups (See Figure XXIII and Table 23)

There was no significant difference between the mean blood volumes in the three groups at 8 - 11 weeks gestation. The mean blood volume in the normotensive group was 4.489 litres ± S.D. 0.999 and that for the hypertension I group was 4.355 litres ± S.D. 0.680; t = 0.455 on 33 degrees of freedom, $0.7 > P > 0.6$. The mean blood volume for the hypertension II group was 4.169 litres ± S.D. 1.200. Comparing this mean with that of the normotensive group gave t = 0.940 on 42 degrees of freedom, $0.4 > P > 0.3$.

The mean blood volume increased steadily from 8 - 11 weeks gestation reaching a maximum at 28 - 31 weeks gestation. The mean increase in the normotensive group during this period was 1.083 litres ± S.D. 0.888. This was a significant increase; t = 5.975 on 24 degrees of freedom, $P < 0.001$.

The mean increase in the hypertension I group was 1.945 litres ± S.D. 0.924; t = 8.931 on 17 degrees of freedom, $P < 0.001$. The mean increase in thehypertension II group was 1.511 litres ± S.D. 0.863; a highly significant increase; t = 8.754 on 24 degrees of freedom, $P < 0.001$. The mean increase in the hypertensive groups combined was greater than that in the normotensive group; t = 2.716 on 65 degrees of freedom, $0.01 > P > 0.001$.

As each individual attained the maximum blood volume at different intervals the maximum blood volume increase was calculated.

The maximum increase in blood volume for the normotensive group was 1.813 litres ± S.D. 0.815; t = 10.889 on 23 degrees of freedom, $P < 0.001$, and occurred on average by the 28th - 31st weeks. The maximum increase in blood volume for the hypertension I group was

## Blood Volume

### All Pregnant Subjects

| Weeks Gestation | Mean Blood Volume | Number of Subjects | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 4.320 | 60 | 1.01 | 0.13 |
| 12 - 15 | 4.655 | 64 | 0.90 | 0.11 |
| 16 - 19 | 4.818 | 60 | 0.81 | 0.10 |
| 20 - 23 | 5.222 | 61 | 0.84 | 0.11 |
| 24 - 27 | 5.497 | 62 | 0.81 | 0.10 |
| 28 - 31 | 5.950 | 60 | 0.72 | 0.09 |
| 32 - 35 | 5.704 | 63 | 0.89 | 0.11 |
| 36 - 39 | 5.750 | 56 | 0.79 | 0.11 |
| 40 & over | 5.665 | 22 | 0.69 | 0.15 |
| (corrected) | 5.734 | | | |
| Post-Delivery | | | | |
| 3rd day | 5.091 | 58 | 0.94 | 0.12 |
| 6 weeks | 4.486 | 63 | 0.82 | 0.10 |
| 12 weeks | 4.425 | 58 | 0.71 | 0.09 |
| 9 months | 4.447 | 30 | 0.86 | 0.16 |
| | 4.297 | | | |

Table 23

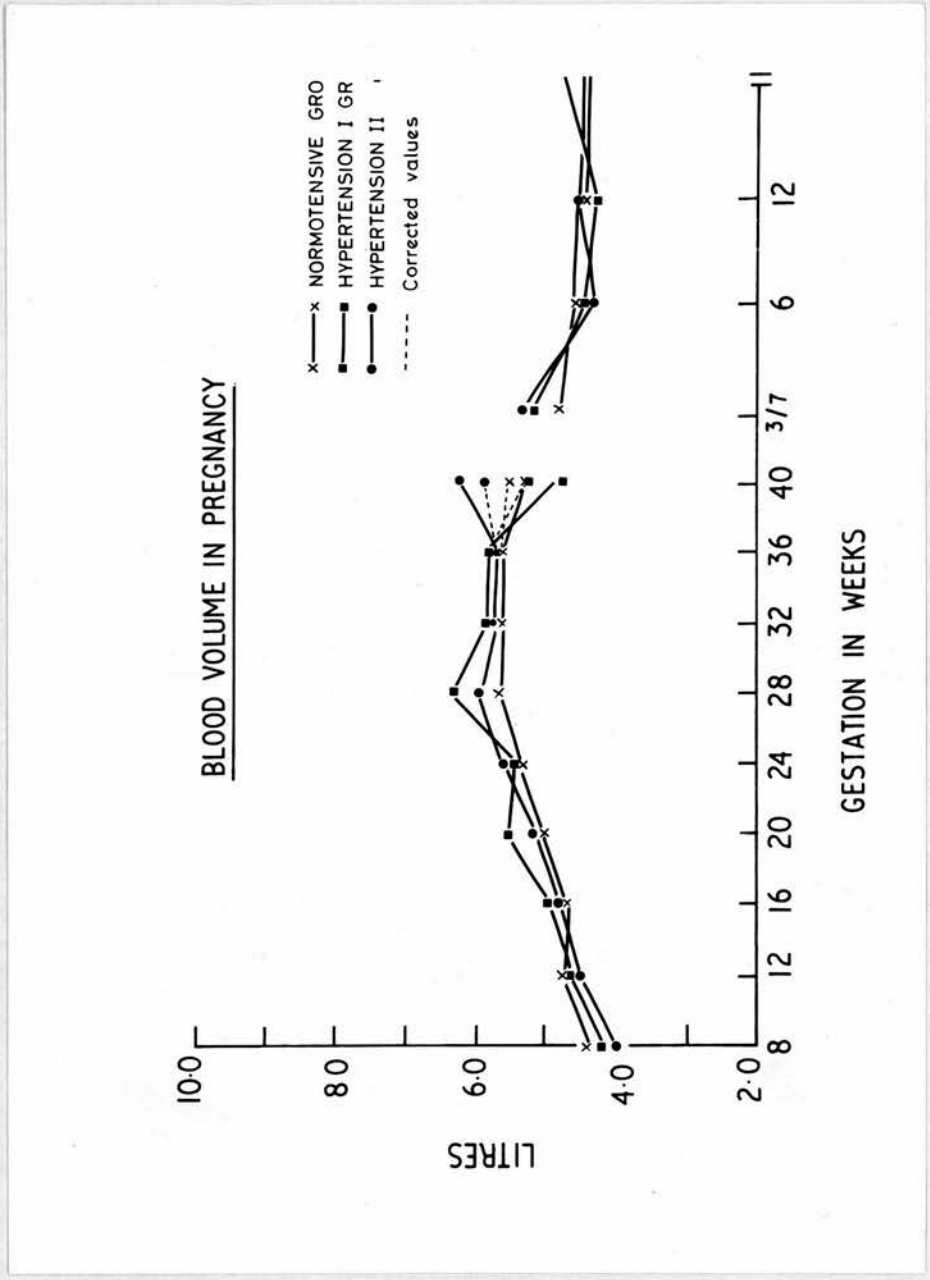



Figure XXIII

Blood volume in pregnancy. The corrected figures are represented by a broken line and closed triangle,

2.023 litres ± S.D. 0.662; t = 12.970 on 17 degrees of freedom, $P < 0.001$; and also occurred on average at 28 - 31 weeks gestation. The maximum increase in blood volume inthe hypertension II group was 2.111 litres ± S.D. 0.778; t = 13.566 on 24 degrees of freedom, $P < 0.001$; and also occurred on average by 28 - 31 weeks gestation.

It is noteworthy that when the maximum increases in blood volume were compared between the groups there were no significant differences. Comparing the normotensive group with the hypertension I group gave t = 0.893 on 40 degrees of freedom, $0.4 > P > 0.3$, and comparing the normotensive group with the hypertension II group gave t = 1.309 on 48 degrees of freedom, $0.2 > P > 0.1$. The mean maximum increase for all groups was 1.980 litres ± S.D. 0.763.

After 28 - 31 weeks gestation the mean blood volume ceased to rise and dropped very slightly towards term. The mean drop from 36 - 39 weeks to 40 weeks and over in all groups was 0.016 litres ± S.D. 0.657.

A more detailed analysis on the normotensive group showed a significant increase between 8 - 11 weeks and 12 - 15 weeks gestation; t = 2.718 on 18 degrees of freedom, $0.02 > P > 0.01$. The mean blood volume at 12 weeks after delivery was not significantly different from the 8 - 11 week figure; t = 0.723 on 17 degrees of freedom, $0.5 > P > 0.4$ and was virtually the same as that at 40 weeks after delivery. From this it was deduced that before 8 weeks gestation there was no significant increase in blood volume but thereafter the increasewas significant. After delivery there was a significant drop in blood volume by the third day of 1.015 litres ± S.D. 0.905; t = 4196 on 13 degrees of freedom and was just not

significantly higher than the 8 - 11 week volume, t = 1.885 on 13 degrees of freedom, $0.1 > P > 0.05$.

Blood Volume Change and Parity

The mean maximum blood volume increase in the 50 primiparous subjects was 1.938 litres $\pm$ S.D. 0.724, and the mean maximum increase for the 17 multiparous patients was 2.107 litres $\pm$ S.D. 0.876. There was no significant difference; t = 0.787 on 65 degreees of freedom, $0.55 > P > 0.4$.

Blood Volume Change and Birth Weight

There was no significant relationship between the maximum increase of blood volume and the birth weight; t = 1.241 on 65 degrees of freedom, $0.3 > P > 0.2$.

Blood Volume Change and Surface Area

There was no significant relationship between the maximum increase in blood volume and surface area at booking; t = 1.477 on 65 degrees of freedom, $0.2 > P > 0.1$.

Blood Volume Change and Change in Weight

There was no relationship between the maximum increase in blood volume and weight gain during pregnancy; t = 0.664 on 65 degrees of freedom, $0.6 > P > 0.5$.

Blood Volume Change and Change of Fore-Arm Flow Rate

There was no significant relationship (See pps. 60 and 83).

Blood Volume Change and Change in Prenanediol

There was no significant relationship between the maximum increase in blood volume and the change in pregnanediol during pregnancy; t = 1.512 on 31 degrees of freedom, $0.2 > P > 0.1$.

## Summary

1. The blood volume was related to surface area, i.e. the larger the surface area, the greater the blood volume.
2. There was no relationship between blood volume and fore-arm flow rate.
3. The blood volume at 8 - 11 weeks gestation was the same as that 6 weeks after delivery.
4. There was a significant increase in blood volume becween 8 - 11 weeks and 12 - 15 weeks gestation.
5. The blood volume continued to increase during pregnancy reaching the maximum at 28 - 31 weeks gestation on average.
6. No significant change occurred after 28 - 31 weeks gestation.
7. The blood volume had fallen almost to first visit levels by the third day after delivery.
8. No relationship was found between change in blood volume during pregnancy and:

    (a) parity
    (b) birth weight
    (c) surface area at first visit
    (d) change in weight
    (e) change in fore-arm flow
    (f) change in pregnanediol.

9. A significant difference was found between the normotensive and hypertensive groups when the change from first visit to 28 - 31 weeks gestation was examined but there was no significant difference between the maximum increases in blood volume for each group. At no other time was there a difference between the three blood-pressure groups.

## HAEMOGLOBIN

### The Control Group

The mean haemoglobin level for 27 non-pregnant subjects was 12.6 G. ± S.D. 0.63 and was calculated from the mean haemoglobin level for each subject.

Reproducibility Between Intervals

Fourteen subjects had haemoglobin readings made in each of six intervals. There was no significant change in haemoglobin from first to sixth interval; $t = 0.514$ on 13 degrees of freedom, $0.7 > P > 0.6$.

### The Pregnant Groups

There was no significant difference between the haemoglobin levels of the three pregnant groups. The mean haemoglobin level during pregnancy was calculated from the mean of each subject and for the normotensive group it was 11.59 G.% ± S.D. 1.07, for the hypertension I group it was 11.68 G.% ± S.D. 1.32 and for the hypertension II group it was 11.55 G.% ± S.D. 1.10. All groups were, therefore, considered together.

Haemoglobin levels during pregnancy showed a quadratic distribution. (The hypothesis that it was not quadratic was rejected; $F = 0.7841$ on 4-77 degrees of freedom, $P > 0.05$)

At 9 - 11 weeks gestation the mean haemoglobin level was 12.2 G.% ± S.D. 0.87 and fell steadily to 20 - 23 weeks gestation when the level was 11.2 G.% ± S.D. 0.79. After 28 - 31 weeks gestation the haemoglobin level began to rise and at 40 weeks gestation was 12.4 G.% ± S.D. 0.78. No significant change occurred

Haemoglobin

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 13.8 | 12.3 | 13.6 | 14.5 | 14.2 | 12.9 |
| No. 2 | 10.8 | 10.2 | 12.4 | 12.3 | 13.6 | 13.6 |
| No. 3 | 12.3 | 12.6 | 13.2 | 12.4 | 12.7 | 13.0 |
| No. 4 | 12.4 | 11.7 | 12.6 | 12.9 | 12.4 | 12.9 |
| No. 5 | 13.0 | 12.1 | 12.4 | 13.3 | 12.6 | 13.3 |
| No. 6 | 13.5 | 12.0 | 11.7 | 12.4 | 13.2 | 13.6 |
| No. 7 | 11.8 | 13.3 | 12.0 | 13.0 | 12.9 | 12.3 |
| No. 8 | 11.4 | 11.7 | 11.0 | 11.0 | 11.8 | 10.7 |
| No. 9 | 12.9 | 13.5 | 13.8 | 13.3 | 13.4 | 13.3 |
| No. 10 | 12.9 | 12.6 | 12.3 | 12.6 | 12.6 | 12.0 |
| No. 11 | 12.6 | 13.9 | 13.9 | 13.5 | 12.9 | 12.6 |
| No. 12 | 13.5 | 12.6 | 13.2 | 13.5 | 12.7 | 13.6 |
| No. 13 | 13.6 | 13.2 | 13.6 | 12.4 | 12.1 | 13.2 |
| No. 14 | 13.6 | 12.3 | 13.8 | 13.8 | 12.7 | 12.9 |
| Mean | 12.72 | 12.43 | 12.82 | 12.92 | 12.84 | 12.85 |

Table 24

Haemoglobin

All Pregnant Groups

| Weeks Gestation | n | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 73 | 12.2 | 0.87 | 0.09 |
| 12 - 15 | 81 | 11.9 | 0.74 | 0.08 |
| 16 - 19 | 82 | 11.5 | 0.69 | 0.08 |
| 20 - 23 | 80 | 11.2 | 0.79 | 0.09 |
| 24 - 27 | 83 | 11.2 | 0.86 | 0.09 |
| 28 - 31 | 83 | 11.3 | 0.77 | 0.08 |
| 32 - 35 | 84 | 11.6 | 0.88 | 0.10 |
| 36 - 39 | 77 | 12.0 | 0.78 | 0.09 |
| 40 & over | 30 | 12.4 | 0.78 | 0.14 |
| (corrected) | | 12.3 | | |
| Post-Delivery | | | | |
| 3 days | 85 | 12.1 | 1.11 | 0.12 |
| 6 weeks | 80 | 12.9 | 0.76 | 0.08 |
| 12 weeks | 69 | 12.7 | 0.78 | 0.09 |
| 40 weeks | 37 | 12.9 | 0.94 | 0.15 |

Table 25

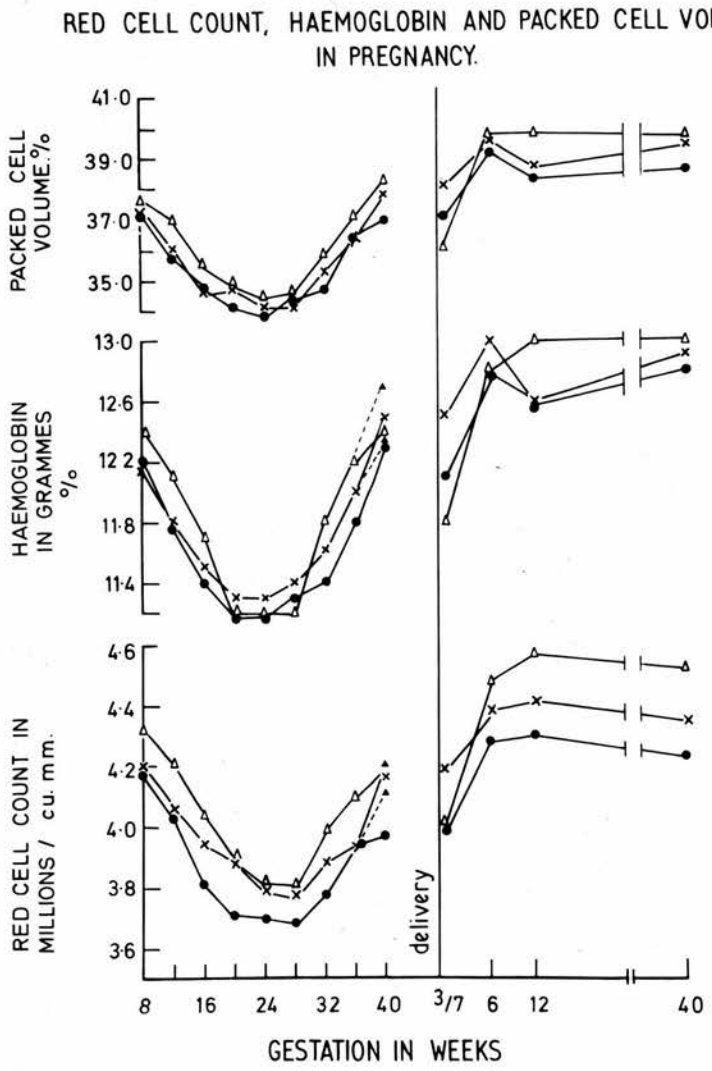



Figure XXIV

The red cell count, haemoglobin and packed cell volume in pregnancy. The corrected figures are represented by an interrupted line and closed triangle.

following delivery and from six weeks post-partum there was a slight rise maintained to 40 weeks post-partum when the haemoglobin was 12.9 G.% ± S.D. 0.94.

The fall from 8 - 11 weeks to 12 - 15 weeks gestation was 0.44 G. ± S.D. 0.64 on average. This was highly significant; $t = 5.759$ on 70 degrees of freedom, $P < 0.001$.

At twelve weeks after delivery the haemoglobin level showed a significant mean rise of 0.48 G.% ± S.D. 0.98 above the first visit level; $t = 3.817$ on 60 degrees of freedom, $P < 0.001$.

Comparison with the Control Group

The mean haemoglobin of the pregnant groups at 8 - 11 weeks gestation was significantly lower than the non-pregnant group; $t = 2.187$ on 98 degrees of freedom, $0.05 > P > 0.02$.

By 40 weeks gestation and throughout the puerperium the haemoglobin levels of the experimental and control groups closely approximated each other.

Supplementary Treatment Received

In the normotensive group 7 patients received parenteral iron therapy and 6 patients received folic acid. In the hypertension I group 8 patients were given parenteral iron and 2 patients folic acid. In the hypertension II group 13 patients were given parenteral iron and nine patients received folic acid.

There was no significant difference in incidence of treatment in the three groups. For parenteral iron therapy $\chi^2 = 0.615$ on 2 degrees of freedom, $0.8 > P > 0.7$ and for folic acid therapy $\chi^2 = 2.760$ on 2 degrees of freedom, $0.3 > P > 0.2$.

## RED CELL COUNT

### The Control Group

The mean red cell count for the 27 non-pregnant subjects was 4.28 m./cu.mm. ± S.D. 0.25 and was calculated from the mean for each subjects. The mean red cell count for the hypertensive and normotensive groups was the same, i.e. 4.28 m./cu.mm.

### Reproducibility Between Intervals

There were 14 subjects in whom readings were obtained in each of six intervals. The change in red cell count from first to sixth intervals was -0.2 ± S.D.030 on average and was just not significant; $t = 2.159$ on 13 degrees of freedom, $0.1 > P > 0.05$.

### The Pregnant Groups (See Figure XXIV)

There was no significant difference between the experimental groups. The mean red cell count during pregnancy for the normotensive group was 3.9 m./cu.mm. ± S.D. 0.05; for the hypertension I group it was 4.0 m./cu.mm. ± S.D. 0.05 and for the hypertension II group it was 3.9 m./cu.mm. ± S.D. 0.05. All groups were, therefore, considered together. The data during pregnancy was of a quadratic distribution. (The hypothesis that the data was not quadratic was rejected; $F = 1.904$ on 7:76 degrees of freedom, $P > 0.05$.)

At 8 - 11 weeks gestation the mean red cell count was 4.23 m./cu.mm. ± S.D. 0.28 and fell steadily to 3.74 m./cu.mm. ± S.D. 0.27 at 28 - 31 weeks gestation. Thereafter, it rose to 4.07 m./cu.mm. ± S.D. 0.30 at 40 weeks gestation. There was no change on the third day after delivery and by six weeks gestation had risen to 4.37 m./cu.mm. ± S.D. 0.34 and remained closely approximate to this level until 40 weeks after delivery.

Red Cell Count

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 4.5 | 4.3 | 4.6 | 4.7 | 4.7 | 4.3 |
| No. 2 | 4.4 | 4.2 | 4.5 | 4.5 | 4.7 | 4.3 |
| No. 3 | 5.1 | 4.8 | 5.2 | 4.8 | 4.4 | 4.6 |
| No. 4 | 4.7 | 4.1 | 4.2 | 4.4 | 4.2 | 4.4 |
| No. 5 | 4.8 | 4.4 | 4.4 | 4.7 | 4.2 | 4.7 |
| No. 6 | 4.4 | 4.1 | 3.8 | 4.1 | 4.4 | 4.8 |
| No. 7 | 4.7 | 4.6 | 4.5 | 4.7 | 4.3 | 4.3 |
| No. 8 | 4.2 | 4.2 | 4.3 | 4.2 | 4.2 | 4.0 |
| No. 9 | 4.3 | 4.3 | 4.4 | 4.5 | 4.5 | 4.8 |
| No. 10 | 4.4 | 5.2 | 4.3 | 4.3 | 4.2 | 4.0 |
| No. 11 | 4.0 | 4.5 | 4.5 | 4.3 | 4.1 | 3.9 |
| No. 12 | 4.2 | 4.0 | 4.1 | 4.4 | 3.9 | 4.0 |
| No. 13 | 4.9 | 4.4 | 4.4 | 4.0 | 4.0 | 4.5 |
| No. 14 | 4.8 | 4.8 | 4.5 | 4.3 | 4.1 | 4.4 |
| | 4.53 | 4.42 | 4.41 | 4.42 | 4.28 | 4.36 |

Table 26

Red Cell Count

All Pregnant Groups

| Weeks Gestation | n | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 67 | 4.23 | 0.28 | 0.03 |
| 12 - 15 | 77 | 4.08 | 0.33 | 0.04 |
| 16 - 19 | 82 | 3.91 | 0.45 | 0.05 |
| 20 - 23 | 79 | 3.81 | 0.33 | 0.04 |
| 24 - 27 | 79 | 3.76 | 0.33 | 0.04 |
| 28 - 31 | 84 | 3.74 | 0.27 | 0.03 |
| 32 - 35 | 84 | 3.86 | 0.35 | 0.04 |
| 36 - 39 | 77 | 3.98 | 0.32 | 0.04 |
| 40 & over | 28 | 4.07 | 0.30 | 0.06 |
| (corrected) | | 4.16 | | |
| Post-Delivery | | | | |
| 3rd day | 82 | 4.06 | 0.36 | 0.04 |
| 6 weeks | 80 | 4.37 | 0.34 | 0.04 |
| 12 weeks | 67 | 4.41 | 0.32 | 0.04 |
| 40 weeks | 37 | 4.35 | 0.33 | 0.05 |

Table 27

The drop from 8 - 11 weeks gestation to 28 - 31 weeks gestation of a mean of 0.47 m./cu.mm. ± S.D. 0.29 was highly significant; $t = 13.173$ on 64 degrees of freedom, $P < 0.001$. The increase from 8 - 11 weeks gestation to 40 weeks after delivery was not significant; $t = 1.762$ on 31 degrees of freedom, $0.1 > P > 0.05$.

Comparison with the Control Group

At 8 - 11 weeks gestation and from 6 weeks post-natally to 40 weeks post-natally the red cell count closely approximated the non-pregnant control level.

## PACKED CELL VOLUME

### The Control Group

The mean packed cell volume for the 27 non-pregnant subjects was 38.51% ± S.D. 1.52 and was calculated from the mean for each subject. There was no significant difference between the normotensive and hypertensive groups; $t = 0.158$ on 25 degrees of freedom, $0.9 > P > 0.8$.

### Reproducibility Between Intervals

From 14 subjects data was available in each of six intervals. There was no significant change from first to sixth intervals; $t = 0.466$ on 13 degrees of freedom, $0.7 > P > 0.6$.

### The Pregnant Groups (See Figure XXIV)

The mean packed cell volume during pregnancy in the normotensive group was 35.10% ± S.D. 0.29, in the hypertension I group it was 35.69% ± S.D. 0.42 and in the hypertension II group it was 34.83% ± S.D. 0.30. There was a significant difference between these means for the normotensive and hypertension I groups; $t = 5.818$ on 48 degrees of freedom, $P < 0.001$, and between the two hypertensive groups; $t = 9.183$ on 57 degrees of freedom, $P < 0.001$.

Throughout pregnancy the packed cell volume of the hypertension I group was the highest and the hypertension II group was the lowest. However, the behaviour of the groups was not significantly different. The data followed a quadratic distribution. (The hypothesis that the data was not quadratic was rejected; $F = 0.5898$ on 4-81 degrees of freedom, $P > 0.05$.)

Packed Cell Volume

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 42.0 | 39.0 | 42.5 | 43.5 | 41.5 | 41.0 |
| No. 2 | 34.0 | 32.5 | 37.0 | 37.0 | 39.5 | 39.0 |
| No. 3 | 39.0 | 38.0 | 40.0 | 36.5 | 37.5 | 38.5 |
| No. 4 | 40.0 | 38.0 | 37.5 | 39.5 | 40.0 | 41.0 |
| No. 5 | 39.0 | 36.5 | 37.0 | 40.0 | 38.0 | 38.5 |
| No. 6 | 41.5 | 38.0 | 37.0 | 36.5 | 40.0 | 42.5 |
| No. 7 | 41.0 | 38.0 | 37.5 | 38.0 | 40.5 | 35.5 |
| No. 8 | 36.0 | 36.0 | 36.5 | 35.0 | 37.0 | 34.5 |
| No. 9 | 40.5 | 41.0 | 42.0 | 39.5 | 41.1 | 42.5 |
| No. 10 | 38.5 | 37.5 | 39.0 | 39.0 | 38.0 | 37.0 |
| No. 11 | 38.0 | 43.0 | 40.0 | 39.0 | 39.0 | 38.0 |
| No. 12 | 40.5 | 38.5 | 41.0 | 39.6 | 39.0 | 39.0 |
| No. 13 | 42.0 | 40.0 | 41.0 | 38.5 | 39.5 | 42.0 |
| No. 14 | 39.0 | 37.5 | 40.0 | 39.5 | 37.0 | 37.0 |
| | 39.36 | 38.11 | 39.14 | 38.65 | 39.11 | 39.00 |

Table 28

## Packed Cell Volume

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. |
| 8 - 11 | 22 | 37.33 | 1.48 | 0.32 | 22 | 37.74 | 3.28 | 0.70 | 29 | 37.40 | 2.61 | 0.48 |
| 12 - 15 | 26 | 36.04 | 2.36 | 0.46 | 23 | 36.96 | 2.53 | 0.53 | 32 | 35.89 | 2.03 | 0.36 |
| 16 - 19 | 25 | 34.64 | 2.06 | 0.41 | 23 | 35.48 | 2.23 | 0.46 | 34 | 34.74 | 1.60 | 0.27 |
| 20 - 23 | 23 | 34.67 | 1.86 | 0.39 | 22 | 34.80 | 2.75 | 0.59 | 35 | 34.11 | 2.14 | 0.36 |
| 24 - 27 | 26 | 34.13 | 2.03 | 0.40 | 23 | 34.39 | 2.62 | 0.55 | 34 | 33.79 | 2.65 | 0.45 |
| 28 - 31 | 26 | 34.10 | 1.95 | 0.38 | 22 | 34.59 | 2.16 | 0.46 | 36 | 34.33 | 2.44 | 0.41 |
| 32 - 35 | 25 | 35.36 | 2.08 | 0.42 | 23 | 35.85 | 2.24 | 0.47 | 36 | 34.65 | 2.86 | 0.48 |
| 36 - 39 | 22 | 36.34 | 2.28 | 0.49 | 23 | 37.13 | 2.64 | 0.55 | 33 | 36.39 | 2.24 | 0.39 |
| 40 & over | 9 | 37.83 | 1.41 | 0.47 | 6 | 38.33 | 3.31 | 1.35 | 15 | 37.00 | 2.28 | 0.59 |
| (corrected) | | 37.40 | | | | 38.46 | | | | 37.32 | | |
| Post-Delivery | | | | | | | | | | | | |
| 3 days | 26 | 38.10 | 2.86 | 0.56 | 24 | 36.23 | 3.40 | 0.69 | 35 | 37.06 | 2.93 | 0.50 |
| 6 weeks | 26 | 39.63 | 1.88 | 0.37 | 23 | 39.78 | 2.29 | 0.48 | 32 | 39.19 | 1.91 | 0.34 |
| 12 weeks | 24 | 38.71 | 1.87 | 0.38 | 18 | 39.83 | 1.39 | 0.33 | 27 | 38.31 | 2.15 | 0.41 |
| 40 weeks | 14 | 39.36 | 1.89 | 0.51 | 10 | 39.65 | 1.93 | 0.61 | 13 | 38.58 | 3.42 | 0.95 |

Table 29

The packed cell volumes of the three groups fell steadily from 8 - 11 weeks gestation to 24 - 27 weeks gestation. The normotensive group fell by a mean of 3.34% ± S.D. 2.30; $t = 6.808$ on 21 degrees of freedom, $P < 0.001$. The hypertension I group fell by 3.31% ± S.D. 2.80; $t = 5.410$ on 20 degrees of freedom, $P < 0.001$ and the hypertension II group fell by 3.72% ± S.D. 3.44; $t = 5.824$ on 28 degrees of freedom, $P < 0.001$. There was no significant difference in the amount of fall shown by the hypertensive groups; $t = 0.449$ on 48 degrees of freedom, $0.7 > P > 0.6$.

After 28 - 31 weeks gestation the packed cell volume for each group rose to first visit levels. On the third day after delivery no significant change occurred in the normotensive and hypertension II groups compared with their 40 week readings but there was a sudden drop in packed cell volume in the hypertension I group which fell below the other two groups for the first and only time. From six weeks post-natally the packed cell volumes resumed their previous order, the hypertension I group being highest and the hypertension II group being the lowest.

At 12 weeks after delivery the normotensive group had increased by 1.0% ± S.D. 2.07 on average over the 8 - 11 week reading; $t = 2.101$ on 18 degrees of freedom, $P = 0.05$. The hypertension I group had increased by 1.56% ± S.D. 2.01 on average over the 8 - 11 week level; $t = 3.193$ on 16 degrees of freedom, $0.01 > P > 0.001$. The increase of 0.90% ± S.D. 2.60 of the hypertension II group over the 8 - 11 week reading was not significant; $t = 1.698$ on 23 degrees of freedom, $0.2 > P > 0.1$.

Comparison with the Control Group

At 8 - 11 weeks gestation the normotensive group was significantly lower than the control level; $t = 2.734$ on 47 degrees of freedom, $0.01 > P > 0.001$. The hypertension I group was not significantly different from the control level; $t = 1.086$ on 47 degrees of freedom, $0.3 > P > 0.2$. The hypertension II group was almost the same as the normotensive group which was significantly lower than the control group.

By 12 weeks after delivery both normotensive and hypertension II groups approximated control levels but the hypertension I group was significantly higher; $t = 2.951$ on 43 degrees of freedom, $0.01 > P > 0.001$.

Summary

The packed cell volume fell during pregnancy to 24 - 27 weeks gestation and then rose to within first visit levels. The normotensive and hypertension II groups were significantly lower than the control group at 8 - 11 weeks gestation but attained these levels after delivery. The hypertension I group behaved in the same manner during and after pregnancy but was consistently higher than the other two groups (apart from the third day reading) starting at 8 - 11 weeks gestation in the same range as the non-pregnant group but attaining significantly higher levels after delivery.

## MEAN CORPUSCULAR HAEMOGLOBIN CONCENTRATION

### The Control Group

The mean M.C.H.C. for 27 of the non-pregnant subjects was 32.59% ± S.D. 0.88 and was calculated from the mean for each subject. There was no significant difference between the normotensive and hypertensive means; $t = 0.914$ on 25 degrees of freedom, $0.4 > P > 0.3$.

### Reproducibility Between Intervals

From 13 subjects readings were available in each of six intervals. There was no significant change from first to sixth interval; $t = 1.161$ on 12 degrees of freedom, $0.3 > P > 0.2$.

### The Pregnant Groups

There was no significant difference in mean cell haemoglobin concentration during pregnancy between the blood pressure groups and no significant change occurred from the beginning of pregnancy to 40 weeks after delivery. All figures closely approximated the non-pregnant control mean.

Mean Corpuscular Haemoglobin Concentration

Control Group; Reproducibility Between Intervals.

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 32.9 | 31.5 | 32.0 | 33.3 | 34.2 | 31.5 |
| No. 2 | 31.8 | 31.4 | 33.5 | 33.2 | 34.4 | 34.9 |
| No. 3 | 31.6 | 33.1 | 33.0 | 34.0 | 33.8 | 33.8 |
| No. 4 | 33.4 | 33.1 | 33.6 | 33.2 | 33.2 | 34.5 |
| No. 5 | 31.0 | 30.8 | 34.1 | 32.6 | 31.0 | 31.5 |
| No. 6 | 32.6 | 31.6 | 31.6 | 34.0 | 32.9 | 32.0 |
| No. 7 | 31.7 | 32.4 | 30.4 | 31.4 | 31.3 | 31.0 |
| No. 8 | 31.9 | 32.9 | 32.9 | 33.7 | 31.1 | 32.5 |
| No. 9 | 33.5 | 33.6 | 31.5 | 32.3 | 33.1 | 33.1 |
| No. 10 | 33.2 | 32.4 | 33.8 | 34.6 | 33.6 | 33.9 |
| No. 11 | 33.3 | 32.7 | 32.9 | 33.3 | 32.6 | 34.9 |
| No. 12 | 32.4 | 33.0 | 33.2 | 32.2 | 30.6 | 31.4 |
| No. 13 | 34.8 | 32.6 | 34.5 | 34.9 | 34.3 | 34.9 |
| Mean | 32.6 | 32.4 | 32.8 | 33.3 | 32.8 | 33.0 |

Table 30

Mean Corpuscular Haemoglobin Concentration

All Pregnant Groups

| Weeks Gestation | n | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 72 | 32.40 | 1.14 | 0.13 |
| 12 - 15 | 80 | 32.74 | 1.25 | 0.14 |
| 16 - 19 | 82 | 32.94 | 1.15 | 0.13 |
| 20 - 23 | 80 | 32.60 | 1.14 | 0.13 |
| 24 - 27 | 83 | 32.98 | 1.16 | 0.13 |
| 28 - 31 | 83 | 32.83 | 1.25 | 0.14 |
| 32 - 35 | 84 | 32.91 | 1.31 | 0.14 |
| 36 - 39 | 77 | 32.82 | 1.14 | 0.13 |
| 40 & over | 30 | 33.02 | 1.16 | 0.21 |
| (corrected) | | 32.98 | | |
| Post-Delivery | | | | |
| 3 days | 85 | 32.62 | 1.13 | 0.12 |
| 6 weeks | 80 | 32.57 | 1.08 | 0.12 |
| 12 weeks | 68 | 32.63 | 1.10 | 0.13 |
| 40 weeks | 37 | 32.89 | 1.10 | 0.18 |

Table 31

## MEAN CELL HAEMOGLOBIN

### The Control Group

The mean M.C.H. for 27 non-pregnant subjects was 29.47 $\mu\mu$g. $\pm$ S.D. 1.50 and was calculated from the mean for each subject. There was no significant difference between the blood pressure groups; $t = 0.384$ on 25 degrees of freedom, $0.8 > P > 0.7$.

### Reproducibility Between Intervals

In 14 subjects readings were obtained in each of six intervals. There was a significant mean increase in M.C.H. from first to sixth intervals of 1.92 $\mu\mu$g. $\pm$ S.D. 2.49; $t = 2.891$ on 13 degrees of freedom, $0.02 > P > 0.01$.

### The Normotensive Group

The mean cell haemoglobin level remained the same from 8 - 11 weeks gestation to 20 - 23 weeks gestation. Thereafter it rose sharply and significantly to 36 - 39 weeks gestation showing a mean increase over first visit levels of 1.57 $\mu\mu$g. $\pm$ S.D. 2.27; $t = 2.934$ on 17 degrees of freedom, $0.01 > P > 0.001$. By the third day after delivery the level had fallen to within first visit levels. At twelve weeks after delivery there was no significant difference from the first visit reading; $t = 0.535$ on 17 degrees of freedom, $0.6 > P > 0.5$.

### The Hypertension I Group

No change occurred in the M.C.H. from 8 - 11 weeks to 20 - 23 weeks gestation. Thereafter there was a mean rise to 36 - 39 weeks gestation of 1.04 $\mu\mu$g. $\pm$ S.D. 1.95 which was significant; $t = 2.258$

Mean Corpuscular Haemoglobin

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 24.1 | 26.2 | 25.4 | 25.8 | 28.9 | 28.2 |
| No. 2 | 24.5 | 24.3 | 27.5 | 27.4 | 29.0 | 31.6 |
| No. 3 | 30.6 | 29.4 | 29.5 | 30.9 | 30.2 | 30.1 |
| No. 4 | 27.6 | 29.5 | 29.5 | 30.3 | 30.0 | 30.3 |
| No. 5 | 28.3 | 26.1 | 28.5 | 27.5 | 28.6 | 28.2 |
| No. 6 | 27.3 | 28.6 | 32.6 | 3222 | 30.9 | 32.3 |
| No. 7 | 27.2 | 27.9 | 25.8 | 26.2 | 28.1 | 26.7 |
| No. 8 | 25.8 | 26.4 | 28.6 | 27.4 | 29.5 | 27.4 |
| No. 9 | 31.5 | 30.9 | 30.0 | 31.4 | 31.5 | 32.3 |
| No. 10 | 27.7 | 30.0 | 30.9 | 31.0 | 30.3 | 29.4 |
| No. 11 | 32.2 | 31.5 | 30.6 | 32.6 | 34.0 | 32.2 |
| No. 12 | 25.5 | 28.7 | 30.6 | 29.6 | 31.5 | 29.3 |
| No. 13 | 29.3 | 24.3 | 28.6 | 29.3 | 30.0 | 31.0 |
| No. 14 | 30.0 | 31.4 | 31.4 | 29.5 | 30,0 | 27.7 |
| Mean | 27.97 | 27.51 | 29.28 | 29.36 | 30.18 | 29.76 |

Table 32

Mean Corpuscular Haemoglobin

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. |
| 8 - 11 | 21 | 29.47 | 1.64 | 0.36 | 19 | 28.72 | 2.12 | 0.49 | 26 | 29.28 | 2.36 | 0.46 |
| 12 - 15 | 25 | 29.28 | 1.88 | 0.38 | 21 | 29.02 | 2.10 | 0.44 | 31 | 29.25 | 1.84 | 0.33 |
| 16 - 19 | 23 | 29.14 | 1.56 | 0.33 | 23 | 29.00 | 1.57 | 0.33 | 33 | 29.88 | 1.53 | 0.27 |
| 20 - 23 | 22 | 29.14 | 1.98 | 0.42 | 22 | 28.85 | 1.52 | 0.32 | 34 | 30.46 | 1.65 | 0.28 |
| 24 - 27 | 23 | 29.77 | 1.90 | 0.40 | 23 | 29.57 | 1.50 | 0.31 | 32 | 30.32 | 1.52 | 0.27 |
| 28 - 31 | 26 | 30.13 | 1.67 | 0.33 | 22 | 29.57 | 2.10 | 0.45 | 33 | 30.42 | 2.01 | 0.35 |
| 32 - 35 | 25 | 30.03 | 1.94 | 0.39 | 23 | 29.83 | 1.85 | 0.39 | 36 | 30.33 | 1.98 | 0.33 |
| 36 - 39 | 21 | 31.09 | 1.31 | 0.29 | 23 | 29.99 | 1.89 | 0.39 | 32 | 30.02 | 1.81 | 0.32 |
| 40 & over | 9 | 30.19 | 2.10 | 0.70 | 4 | 29.40 | 1.47 | 0.74 | 14 | 30.89 | 1.56 | 0.42 |
| (corrected) | | 29.48 | | | | 29.94 | | | | 29.98 | | |
| Post-Delivery | | | | | | | | | | | | |
| 3 days | 24 | 29.62 | 1.64 | 0.34 | 24 | 29.60 | 2.14 | 0.44 | 35 | 29.41 | 5.58 | 0.94 |
| 6 weeks | 25 | 29.71 | 1.96 | 0.39 | 23 | 28.83 | 2.09 | 0.44 | 31 | 30.08 | 2.19 | 0.39 |
| 12 weeks | 23 | 28.77 | 2.64 | 0.55 | 18 | 28.56 | 2.02 | 0.48 | 25 | 29.28 | 2.05 | 0.41 |
| 40 weeks | 14 | 29.55 | 1.26 | 0.34 | 10 | 28.89 | 1.73 | 0.55 | 13 | 30.20 | 1.65 | 0.46 |

Table 33

on 17 degrees of freedom, $0.05 > P > 0.02$. After delivery the M.C.H. fell to first visit levels and at 12 weeks after delivery there was no significant difference from the first visit reading; $t = 0.955$ on 14 degrees of freedom, $0.4 > P > 0.3$.

The Hypertension II Group

No change occurred in the M.C.H. from 8 - 11 weeks to 12 - 15 weeks gestation but there was a significant mean rise of 1.33 µµg. ± S.D. 2.39 from 12 - 15 weeks to 20 - 23 weeks gestation; $t = 2.722$ on 23 degrees of freedom, $0.02 > P > 0.01$. Thereafter, the level was maintained to 36 - 39 weeks gestation. By 12 weeks after delivery there was no difference from the first visit level.

Relationship Between the Experimental Groups

From 16 - 19 weeks gestation to 32 - 35 weeks gestation and throughout the puerperium the M.C.H. of the Hypertension II group was higher than the other two groups. The hypertension II group rose significantly eight weeks earlier than the other two groups but there was no significant difference in the amount of rise shown by the three groups. For example, comparing the smallest rise, in the hypertension I group, with the largest increase, in the normotensive group, gave $t = 0.752$ on 34 degrees of freedom, $0.5 > P > 0.4$.

Comparison with the Control Group

The control group showed a mean rise of 1.92 µµg. ± S.D. 2.49 over six intervals. This began at the third interval, equivalent to 16 - 19 weeks gestation in the pregnant groups. The degree of rise was similar to that in the pregnant groups although occurring at a different time interval and beginning at a lower level.

It is difficult to draw any conclusions from such findings. The non-pregnant control group was not followed long enough to confirm or refute the fact that the post-natal decline in M.C.H. in the experimental groups may be a spurious finding.

## MEAN CELL VOLUME

### The Control Group

The mean cell volume of 27 non-pregnant subjects was 90.4 cμ. ± S.D. 4.96 and was calculated from the mean for each subject. There was no significant difference between the means of the normotensive and hypertensive groups; $t = 0.063$ on 25 degrees of freedom.

### Reproducibility Between Intervals

From 15 subjects data was available in each of six intervals. There was a mean increase in mean cell volume of 4.47 cμ. ± S.D. 4.75 from first to sixth intervals; $t = 3.645$ on 14 degrees of freedom, $0.01 > P > 0.001$.

### The Pregnant Groups

In the normotensive group no significant change occurred from 8 - 11 weeks to 16 - 19 weeks gestation. Following this there was a mean rise of 3.28 cμ. ± S.D. 5.36 to 36 - 39 weeks gestation; $t = 2.598$ on 17 degrees of freedom, $0.02 > P > 0.01$. Similarly, the hypertension I group showed no significant change from 8 - 11 weeks to 16 - 19 weeks gestation. Following this there was a rise to 28 - 31 weeks gestation of a mean of 1.82 cμ. ± S.D. 4.25 which was just not significant; $t = 1.767$ on 16 degrees of freedom, $0.1 > P > 0.05$. The hypertension II group showed a mean rise from 8 - 11 weeks gestation to 20 - 23 weeks gestation of 2.58 cμ. ± S.D. 4.82; $t = 2.620$ on 23 degrees of freedom; $0.02 > P > 0.01$; after which there was little further increase. At 12 weeks after delivery all pregnant groups showed a fall to first visit levels.

## Mean Cell Volume

### Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 93 | 93 | 92 | 93 | 88 | 95 |
| No. 2 | 77 | 77 | 82 | 82 | 84 | 91 |
| No. 3 | 77 | 79 | 77 | 76 | 85 | 84 |
| No. 4 | 83 | 89 | 88 | 91 | 91 | 88 |
| No. 5 | 83 | 86 | 85 | 84 | 95 | 87 |
| No. 6 | 86 | 90 | 96 | 98 | 97 | 98 |
| No. 7 | 86 | 86 | 85 | 84 | 88 | 86 |
| No. 8 | 94 | 96 | 96 | 88 | (92.6) | 89 |
| No. 9 | 88 | 72 | 91 | 91 | 91 | 93 |
| No. 10 | 95 | 96 | 89 | 91 | 95 | 97 |
| No. 11 | (96.8) | 97 | 96 | 93 | 100 | 98 |
| No. 12 | 86 | 91 | 93 | 96 | 99 | 94 |
| No. 13 | 78 | 83 | 88 | 86 | 90 | 85 |
| No. 14 | 81 | 81 | 84 | 86 | 83 | (83.0) |
| No. 15 | 86 | 87 | 91 | 91 | 91 | (89.2) |
| Mean | 85.99 | 86.87 | 88.87 | 88.67 | 91.31 | 90.48 |

Table 34

Note

Data were missing on four occasion in these cases. The mean reading for the subject was inserted in the Table and these figures are given in brackets.

## Mean Cell Volume

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. | n | Mean | S.D. | S.E. |
| 8 - 11 | 21 | 89.57 | 4.42 | 0.97 | 19 | 88.95 | 4.60 | 1.06 | 26 | 86.74 | 5.75 | 1.13 |
| 12 - 15 | 25 | 89.28 | 5.70 | 1.14 | 21 | 88.29 | 5.28 | 1.15 | 31 | 88.90 | 4.95 | 0.89 |
| 16 - 19 | 23 | 88.17 | 4.25 | 0.89 | 23 | 88.09 | 4.19 | 0.87 | 34 | 91.35 | 4.65 | 0.80 |
| 20 - 23 | 22 | 89.91 | 5.34 | 1.14 | 22 | 90.00 | 4.12 | 0.88 | 34 | 92.53 | 4.17 | 0.72 |
| 24 - 27 | 23 | 90.26 | 5.44 | 1.13 | 23 | 90.39 | 4.65 | 0.97 | 32 | 91.44 | 4.17 | 0.74 |
| 28 - 31 | 26 | 90.54 | 4.38 | 0.86 | 22 | 90.91 | 4.78 | 1.02 | 33 | 92.79 | 5.09 | 0.89 |
| 32 - 35 | 25 | 91.08 | 4.99 | 1.00 | 23 | 90.26 | 5.06 | 1.06 | 36 | 92.25 | 5.68 | 0.95 |
| 36 - 39 | 22 | 92.68 | 3.88 | 0.83 | 23 | 90.96 | 4.53 | 0.95 | 32 | 92.38 | 5.03 | 0.89 |
| 40 & over | 9 | 91.11 | 5.11 | 1.70 | 4 | 91.00 | 4.24 | 2.12 | 15 | 93.07 | 3.71 | 0.96 |
| (corrected) | | 89.90 | | | | 89.46 | | | | 91.25 | | |
| Post-Delivery | | | | | | | | | | | | |
| 3 days | 24 | 90.83 | 4.59 | 0.94 | 24 | 90.67 | 5.58 | 1.14 | 34 | 92.59 | 5.32 | 0.91 |
| 6 weeks | 25 | 90.84 | 5.06 | 1.01 | 23 | 89.74 | 5.44 | 1.13 | 32 | 91.81 | 5.28 | 0.93 |
| 12 weeks | 23 | 87.96 | 6.55 | 1.37 | 18 | 87.44 | 4.91 | 1.16 | 25 | 89.76 | 5.58 | 1.12 |
| 40 weeks | 14 | 90.64 | 3.48 | 0.93 | 10 | 87.90 | 4.28 | 1.35 | 13 | 91.31 | 4.48 | 1.24 |
| (corrected) | | 88.81 | | | | 89.14 | | | | 90.68 | | |

Table 35

Relationship Between the Pregnant Groups

The hypertension II group had the lowest M.C.V. at 8 - 11 weeks gestation but it rose rapidly to 20 - 23 weeks gestation and remained higher than the other two pregnant groups throughout. In the normotensive and hypertension I groups the increase in mean cell volume was delayed to after 16 - 19 weeks gestation. There was a significant difference between the hypertension II group and the normotensive group at 16 - 19 weeks gestation; $t = 2.596$ on 55 degrees of freedom, $0.05 > P > 0.01$.

Comparison with the Control Group

The control group showed a significant increase from first to sixth intervals, the rise beginning from the first visit. The pregnant groups showed similar increases although occurring at different intervals. As in the case of the mean corpuscular haemoglobin data, it is difficult to draw any firm conclusion from these readings, as sufficient numbers of the non-pregnant group were not followed long enough to confirm or refute the findings of a fall after delivery.

## WHITE CELL COUNT

### The Control Group

The mean white cell count in 27 non-pregnant subjects was 6.95 thousand/cu.mm. ± S.D. 1.05 and was calculated from the mean for each subject. The mean white cell count for the normotensive subjects was 6.76 thousand/cu.mm. ± S.D. 1.10 and that for the hypertensive subjects was 7.34 thousand/cu.mm. ± S.D. 0.87. There was no significant difference between these two means; $t = 1.371$ on 25 degrees of freedom, $0.2 > P > 0.1$.

### Reproducibility Between Intervals

Fourteen subjects had readings available in each of the six intervals. The mean for the first interval was 7.61 thousand per cu.mm. and for the sixth interval was 7.60 thousand/cu.mm.

### The Pregnant Groups

There was no significant difference between the blood pressure groups. The mean white cell count during pregnancy for the normotensive group was 8.90 thousand/cu.mm. ± S.D. 1.45, for the hypertension I group it was 9.55 thousand/cu.mm. ± S.D. 1.77 and for the hypertension II group it was 9.18 thousand/cu.mm. ± S.D. 1.36. Comparing the normotensive group with the hypertension I group gave $t = 1.362$ on 44 degrees of freedom, $0.2 > P > 0.1$.

For further analysis the groups were, therefore, considered together.

There was a significant increase in white cell count from 8 - 11 weeks to 32 - 35 weeks gestation of 1.26 thousand/cu.mm. ±

White Cell Count

Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 10.0 | 7.0 | 7.0 | 7.0 | 6.0 | 9.0 |
| No. 2 | 6.0 | 5.0 | 5.0 | 6.0 | 6.0. | 5.0 |
| No. 3 | 8.0 | 6.0 | 11.0 | 9.0 | 6.0 | 8.0 |
| No. 4 | 10.0 | 9.0 | 6.0 | 7.0 | 7.0 | 10.0 |
| No. 5 | 8.0 | 6.0 | 7.0 | 7.0 | 6.0 | 7.0 |
| No. 6 | 7.0 | 8.0 | 6.0 | 8.0 | 9.0 | 10.0 |
| No. 7 | 7.5 | 9.0 | 10.0 | 10.0 | 8.0 | 8.0 |
| No. 8 | 5.0 | 5.0 | 7.0 | 7.0 | 5.0 | 5.0 |
| No. 9 | 8.0 | 8.0 | 8.0 | 9.0 | 8.4 | 9.0 |
| No. 10 | 7.0 | 9.0 | 9.0 | 9.0 | 9.0 | 7.0 |
| No. 11 | 6.0 | 9.0 | 6.0 | 7.0 | 7.0 | 6.0 |
| No. 12 | 9.0 | 9.0 | 10.0 | 7.0 | 7.0 | 8.4 |
| No. 13 | 8.0 | 6.0 | 7.0 | 7.5 | 6.0 | 7.0 |
| No. 14 | 7.0 | 6.0 | 7.0 | 7.0 | 6.0 | 7.0 |
| Mean | 7.61 | 7.29 | 7.57 | 7,68 | 6.89 | 7.60 |

Table 36

White Cell Count

| Weeks Gestation | n | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 54 | 8.50 | 1.83 | 0.25 |
| 12 - 15 | 63 | 8.46 | 2.10 | 0.26 |
| 16 - 19 | 66 | 8.84 | 2.00 | 0.25 |
| 20 - 23 | 64 | 9.34 | 2.25 | 0.28 |
| 24 - 27 | 67 | 9.20 | 2.19 | 0.27 |
| 28 - 31 | 70 | 9.51 | 2.08 | 0.25 |
| 32 - 35 | 70 | 9.74 | 2.14 | 0.26 |
| 36 - 39 | 63 | 9.33 | 2.34 | 0.29 |
| 40 & over | 23 | 9.30 | 2.16 | 0.45 |
| (corrected) | | 9.51 | | |
| Post-Delivery | | | | |
| 3 days | 69 | 10.83 | 3.34 | 0.40 |
| 6 weeks | 74 | 7.05 | 1.88 | 0.22 |
| 12 weeks | 66 | 6.98 | 1.52 | 0.19 |
| 40 weeks | 36 | 6.83 | 1.68 | 0.28 |

Table 37

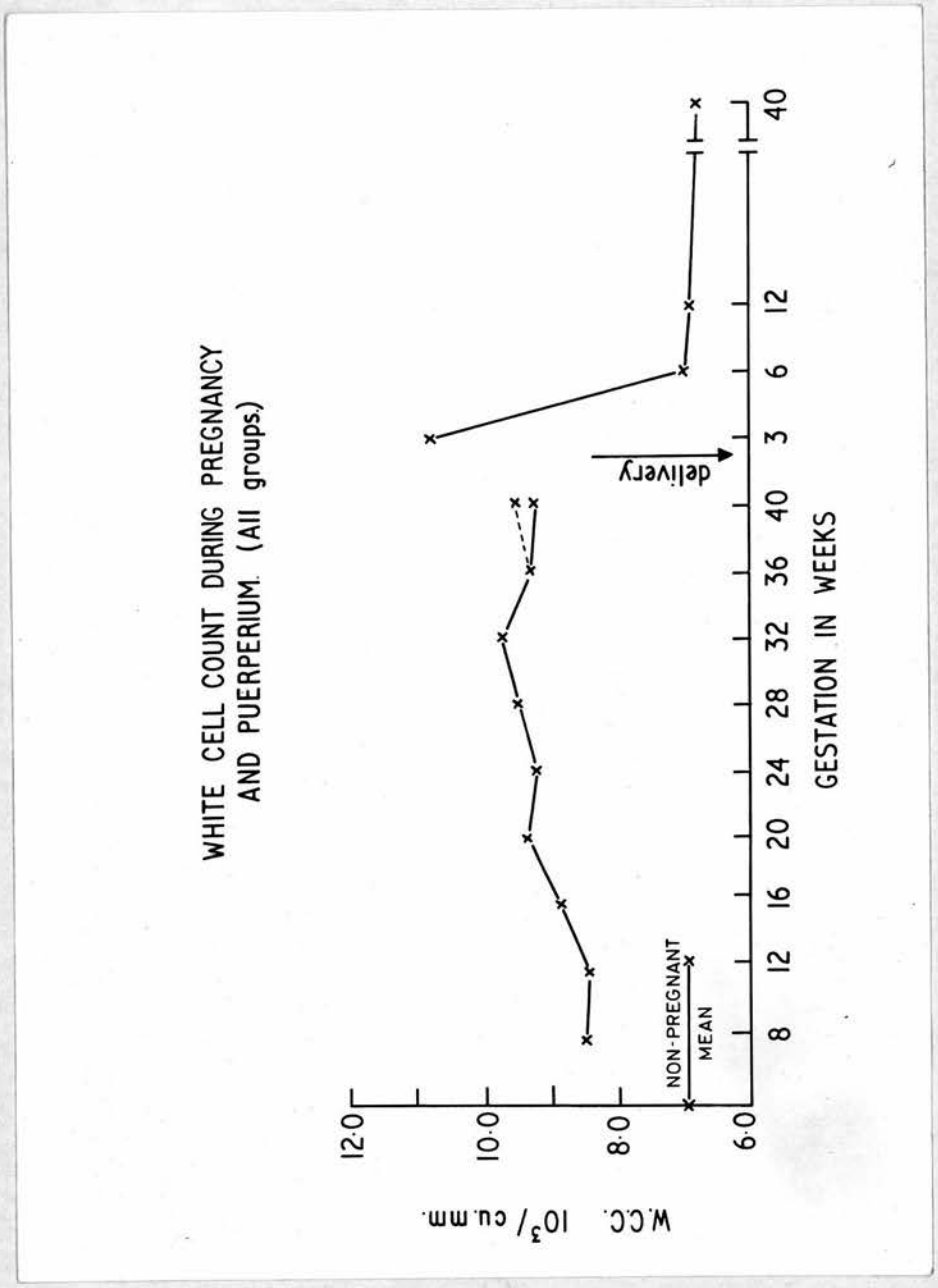



**Figure XXV**

The white cell count in pregnancy.

S.D. 2.15 on average; t = 4.258 on 52 degrees of freedom, $P < 0.001$. After 32 - 35 weeks there was a very slight drop.

On the third day after delivery the white cell count had significantly increased over the 36 - 39 week level by a mean of 1.68 thousand/cu.mm. $\pm$ S.D. 3.26; t = 3.926 on 57 degrees of freedom, $P < 0.001$. Following this there was a mean fall below first visit levels; 1.75 thousand/cu.mm. $\pm$ S.D. 1.88; t = 6.356 on 46 degrees of freedom, $P < 0.001$.

Comparison with the Control Group

At 8 - 11 weeks gestation the mean white cell count of the pregnant groups was significantly higher than the non-pregnant mean; t = 4.070 on 79 degrees of freedom, $P < 0.001$. The disparity increased during pregnancy. By six weeks after delivery the white cell count closely approximated the non-pregnant mean and remained at this level to 40 weeks post-delivery.

Summary

At 8 - 11 weeks gestation the mean white cell count was already significantly higher than the non-pregnant levels. There was a further steady rise during pregnancy reaching a peak at 32 - 35 weeks gestation. A further significant increase occurred in the early post-partum period but by six weeks post-delivery the white cell count had fallen to non-pregnant levels. It is noteworthy that during pregnancy the highest level attained was 9.74 thousand per cu.mm. $\pm$ S.D. 2.14 and the 99% upper confidence limit was 10.41 thousand per cu.mm.

## BODY WEIGHT

### The Control Group

The mean weight for the 32 non-pregnant subjects was 134.79 lbs. ± S.D. 16.09.

The mean weight for the 22 normotensive subjects was 132.20 lbs. ± S.D. 14.65 which was not significantly lower than the 10 hypertensive subjects which was 140.50 lbs. ± S.D. 18.40; $t = 1.371$ on 30 degrees of freedom, $0.2 > P > 0.1$.

### Reproducibility Between Intervals

Fourteen subjects were weighed in each of 6 intervals. There was a significant mean increase of 2.44 lbs. ± S.D. 2.80 from first to sixth intervals; $t = 3.262$ on 13 degrees of freedom, $0.01 > P > 0.001$.

### The Pregnant Groups

All experimental groups behaved similarly and were analysed as one group. There was no significant difference between the mean weights at 8 - 11 weeks gestation. For example, the normotensive group weighed 123.33 lbs. ± S.D. 14.93 which was not different from the hypertension II group which weighed 126.20 lbs. ± S.D. 12.41; $t = 0.756$ on 50 degrees of freedom, $0.5 > P > 0.4$.

There was a steady increase in weight from 8 - 11 weeks gestation to term, the mean weight gain for all groups was 22.31 lbs. ± S.D. 7.02; $t = 29.460$ on 85 degrees of freedom, $P < 0.001$. The mean increase for the normotensive group was 22.08 lbs. ± S.D. 8.17, that for the hypertension I group was 22.54 lbs. ± S.D. 5.78 and for the hypertension II group it was 22.35 lbs. ± S.D. 7.07. There was no significant difference between these increases, e.g. comparing the normotensive with the hypertension I group $t = 0.310$ on

## Weight

### Control Group; Reproducibility Between Intervals

| Subjects | Intervals | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| No. 1 | 119.00 | 121.00 | 121.88 | 120.25 | 121.50 | 121.75 |
| No. 2 | 117.50 | 117.00 | 119.75 | 116.00 | 117.00 | 117.00 |
| No. 3 | 147.00 | 150.88 | 149.38 | 151.00 | 154.00 | 154.44 |
| No. 4 | 129.13 | 129.13 | 129.38 | 128.25 | 128.75 | 130.00 |
| No. 5 | 143.56 | 145.25 | 145.50 | 144.44 | 142.38 | 142.50 |
| No. 6 | 153.81 | 155.75 | 157.06 | 162.75 | 156.50 | 154.75 |
| No. 7 | 131.44 | 131.50 | 132.88 | 134.50 | 136.13 | 135.75 |
| No. 8 | 132.00 | 132.00 | 133.00 | 134.00 | 134.00 | 134.00 |
| No. 9 | 112.00 | 115.88 | 113.63 | 113.16 | 113.38 | 113.88 |
| No. 10 | 120.75 | 121.13 | 122.88 | 122.38 | 123.13 | 123.50 |
| No. 11 | 114.50 | 115.50 | 116.25 | 116.25 | 117.25 | 117.25 |
| No. 12 | 158.13 | 158.00 | 163.25 | 164.50 | 159.63 | 158.25 |
| No. 13 | 169.00 | 171.56 | 170.50 | 168.50 | 171.00 | 170.13 |
| No. 14 | 135.00 | 141.50 | 146.06 | 146.00 | 141.00 | 143.75 |
| Mean | 134.49 | 136.15 | 137.24 | 137.28 | 136.83 | 136.93 |

Table 38

## Weight

### All Pregnant Groups

| Weeks Gestation | n | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 74 | 125.24 | 13.61 | 1.58 |
| 12 - 15 | 81 | 126.89 | 13.79 | 1.53 |
| 16 - 19 | 82 | 130.85 | 15.36 | 1.70 |
| 20 - 23 | 83 | 135.45 | 15.19 | 1.67 |
| 24 - 27 | 84 | 138.82 | 14.97 | 1.63 |
| 28 - 31 | 86 | 142.24 | 15.15 | 1.63 |
| 32 - 35 | 86 | 145.09 | 15.40 | 1.66 |
| 36 - 39 | 84 | 147.30 | 15.14 | 1.65 |
| 40 & over | 45 | 149.32 | 14.51 | 2.16 |
| Post-Delivery | | | | |
| 3 days | 51 | 138.72 | 15.73 | 2.20 |
| 6 weeks | 74 | 129.62 | 14.29 | 1.66 |
| 12 weeks | 62 | 128.92 | 16.96 | 2.15 |
| 40 weeks | 39 | 127.75 | 15.72 | 2.52 |

Table 39

48 degrees of freedom, $0.8 > P > 0.7$.

After delivery the weight fell rapidly and at 40 weeks after delivery the mean weight was only 2.74 lbs. $\pm$ S.D. 6.79 greater than the first visit level; $t = 2.485$ on 37 degrees of freedom, $0.02 > P > 0.01$.

Comparison with the Control Group

The control group weighed 9.55 lbs. more than the pregnant group at 8 - 11 weeks gestation; $t = 3.135$ on 104 degrees of freedom, $P < 0.001$, but not at 12 - 15 or 16 - 19 weeks gestation. By 12 weeks after delivery there was no significant difference between the control and experimental groups; $t = 1.617$ on 92 degrees of freedom, $0.2 > P > 0.1$.

Summary

There was no significant difference in the mean weights or mean weight gain during pregnancy between the blood pressure groups. The overall mean weight gain was 22.31 lbs. $\pm$ S.D. 7.02.

The control group weighed more than the pregnant group at 8 - 11 weeks gestation but this significant difference did not recur even after delivery. The mean weight gain of 2.44 lbs. in the control group over 6 intervals was significant.

By 40 weeks after delivery the experimental groups weighed 2.74 lbs. more than at booking.

During pregnancy weight gain was controlled by diet in all subjects.

## PREGNANEDIOL

Pregnanediol excretion was measured from 24 or 48 hour specimens of urine collected every four weeks in 34 subjects. A total of 261 estimations were made. Eight of the subjects were normotensive, 12 were included in the hypertension I group and 14 in the hypertension II group.

### Results

There was no significant difference in the increase in pregnanediol excretion during pregnancy in the three blood pressure groups. The excretion of the normotensive group increased by a mean of 30.83 mg.% $\pm$ S.D. 14.47, that of the hypertension I group increased by 43.23 mg.% $\pm$ S.D. 12.22 and that of the hypertension II group increased by 38.71 mg.% $\pm$ S.D. 23.13. Comparing the change between normotensive and hypertension I groups gave $t = 2.023$ on 17 degrees of freedom, $0.1 > P > 0.05$.

For the rest of the analysis the groups were considered together

A significant increase occurred between 8 - 11 weeks and 12 - 15 weeks gestation of 4.06 mg.% $\pm$ S.D. 5.25; $t = 3.867$ on 24 degrees of freedom, $P < 0.001$. Thereafter, the pregnanediol excretion increased rapidly until term was approached when there was a decrease in the rate of increase. The mean total increase from first visit to term was 35.59 mg.% $\pm$ S.D. 19.70; $t = 10.535$ on 33 degrees of freedom, $P < 0.001$.

At six weeks after delivery the pregnanediol excretion was significantly lower than that at first visit by a mean of 9.21 mg.% $\pm$ S.D. 5.76; $t = 6.394$ on 15 degrees of freedom, $P < 0.001$.

### Relationship to Change in Flow Rate

See page 85 .

Pregnanediol

All Pregnant Groups

| Weeks Gestation | n | Mean | S.D. | S.E. |
|---|---|---|---|---|
| 8 - 11 | 27 | 11.06 | 4.55 | 0.88 |
| 12 - 15 | 31 | 13.89 | 5.02 | 0.90 |
| 16 - 19 | 27 | 18.46 | 7.76 | 1.49 |
| 20 - 23 | 27 | 23.64 | 9.66 | 1.86 |
| 24 - 27 | 30 | 31.73 | 14.72 | 2.69 |
| 28 - 31 | 27 | 42.13 | 17.33 | 2.57 |
| 32 - 35 | 29 | 53.15 | 17.48 | 3.25 |
| 36 - 39 | 26 | 47.79 | 16.02 | 3.14 |
| 40 & over | 7 | 54.51 | 22.31 | 8.43 |
| (corrected) | | 50.02 | | |
| Post-Delivery | | | | |
| 3 days | 2 | 3.10 | 0.14 | 0.10 |
| 6 weeks | 19 | 2.44 | 1.94 | 0.45 |
| 12 weeks | 9 | 2.68 | 1.18 | 0.39 |

Table 40

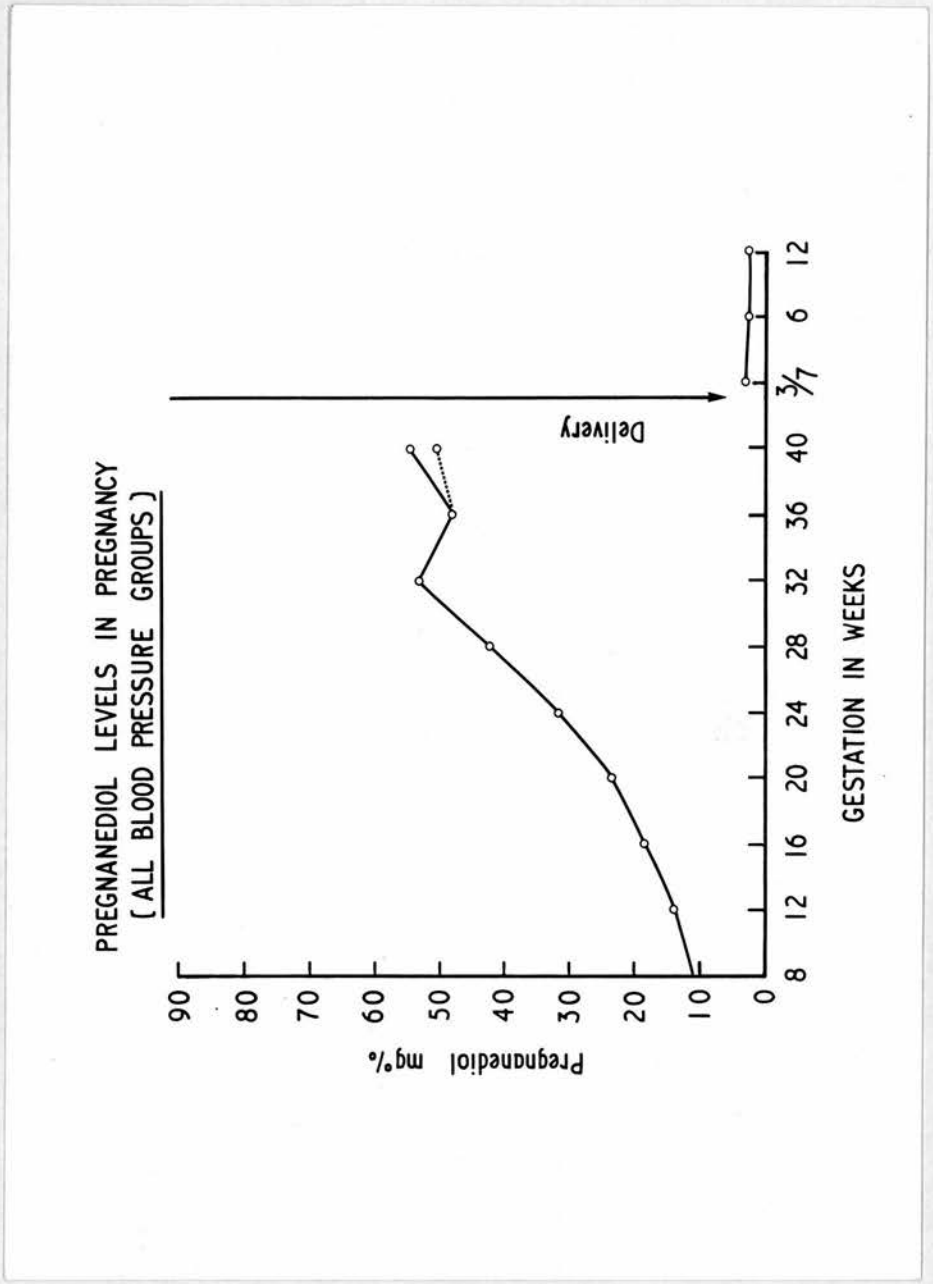



Figure XXVI

Pregnanediol excretion levels in pregnancy. The corrected figure is shown by the dotted line and open circle.

## CORNIFICATION INDEX

A total of 762 measurements was obtained.

### Results

By 8 - 11 weeks gestation the mean cornification index was 5.16 ± S.D. 5.27 below the last post-natal reading; $t = 7.831$ on 64 degrees of freedom, $P < 0.001$.

From 8 - 11 weeks to 32 - 35 weeks gestation the mean cornification index fell by 2.9 ± S.D. 4.31 in the normotensive group, 2.3 ± S.D. 3.83 in the hypertension I group and 2.6 ± S.D. 3.97 in the hypertension II group. All were significant falls and did not significantly differ from each other, e.g. normotensive decrease compared with hypertension I decrease gave $t = 0.527$ on 48 degrees of freedom, $0.7 > P > 0.6$. The pregnant groups were therefore analysed together. The mean fall was 2.63 ± S.D. 4.00; $t = 6.097$ on 85 degrees of freedom, $P < 0.001$. No significant change occurred from 36 - 39 weeks to 40 weeks and over. There was a mean rise of 0.5 ± S.D. 1.79; $t = 1.540$ on 27 degrees of freedom, $0.2 > P > 0.1$.

Readings were not available on the third day after delivery but the cornification index had greatly increased over the first visit reading by 6 weeks after delivery.

### Relationship with Fore-Arm Flow

See page 86.

Table 41

| Weeks Gestation | Normotensive | | | | Hypertension I | | | | Hypertension II | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | No. | S.D. | S.E. | Mean | No. | S.D. | S.E. | Mean | No. | S.D. | S.E. |
| 8 - 11 | 3.41 | 20 | 4.91 | 1.10 | 3.04 | 21 | 3.19 | 0.70 | 4.74 | 25 | 4.94 | 0.99 |
| 12 - 15 | 3.52 | 25 | 5.06 | 1.01 | 3.98 | 20 | 5.81 | 1.30 | 2.47 | 31 | 3.57 | 0.64 |
| 16 - 19 | 3.23 | 22 | 5.23 | 1.11 | 2.94 | 22 | 3.03 | 0.65 | 2.12 | 33 | 4.50 | 0.78 |
| 20 - 23 | 2.42 | 25 | 4.15 | 0.83 | 1.27 | 22 | 2.18 | 0.46 | 2.59 | 35 | 3.85 | 0.65 |
| 24 - 27 | 2.48 | 26 | 4.00 | 0.78 | 1.00 | 22 | 1.60 | 0.34 | 1.69 | 34 | 3.94 | 0.67 |
| 28 - 31 | 1.26 | 25 | 2.07 | 0.41 | 1.55 | 21 | 1.80 | 0.39 | 1.16 | 32 | 2.63 | 0.46 |
| 32 - 35 | 1.05 | 22 | 1.56 | 0.33 | 0.70 | 22 | 1.61 | 0.34 | 1.13 | 31 | 2.51 | 0.45 |
| 36 - 39 | 0.98 | 22 | 1.82 | 0.39 | 0.91 | 22 | 2.06 | 0.44 | 1.61 | 32 | 3.10 | 0.55 |
| 40 & over | 0.44 | 9 | 0.98 | 0.33 | 1.70 | 5 | 1.44 | 0.64 | 2.36 | 14 | 3.95 | 1.06 |
| (corrected) | 0.87 | | | | 1.91 | | | | 2.36 | | | |
| Post-Delivery | | | | | | | | | | | | |
| 6 weeks | 5.08 | 19 | 5.67 | 1.30 | 6.10 | 20 | 4.89 | 1.09 | 7.46 | 24 | 6.13 | 1.25 |
| 12 weeks | 6.00 | 16 | 5.47 | 1.37 | 7.46 | 13 | 4.01 | 1.11 | 9.58 | 18 | 6.04 | 1.42 |
| 40 weeks | 7.00 | 8 | 11.57 | 4.09 | 9.00 | 1 | - | - | 4.60 | 3 | 4.29 | 2.48 |

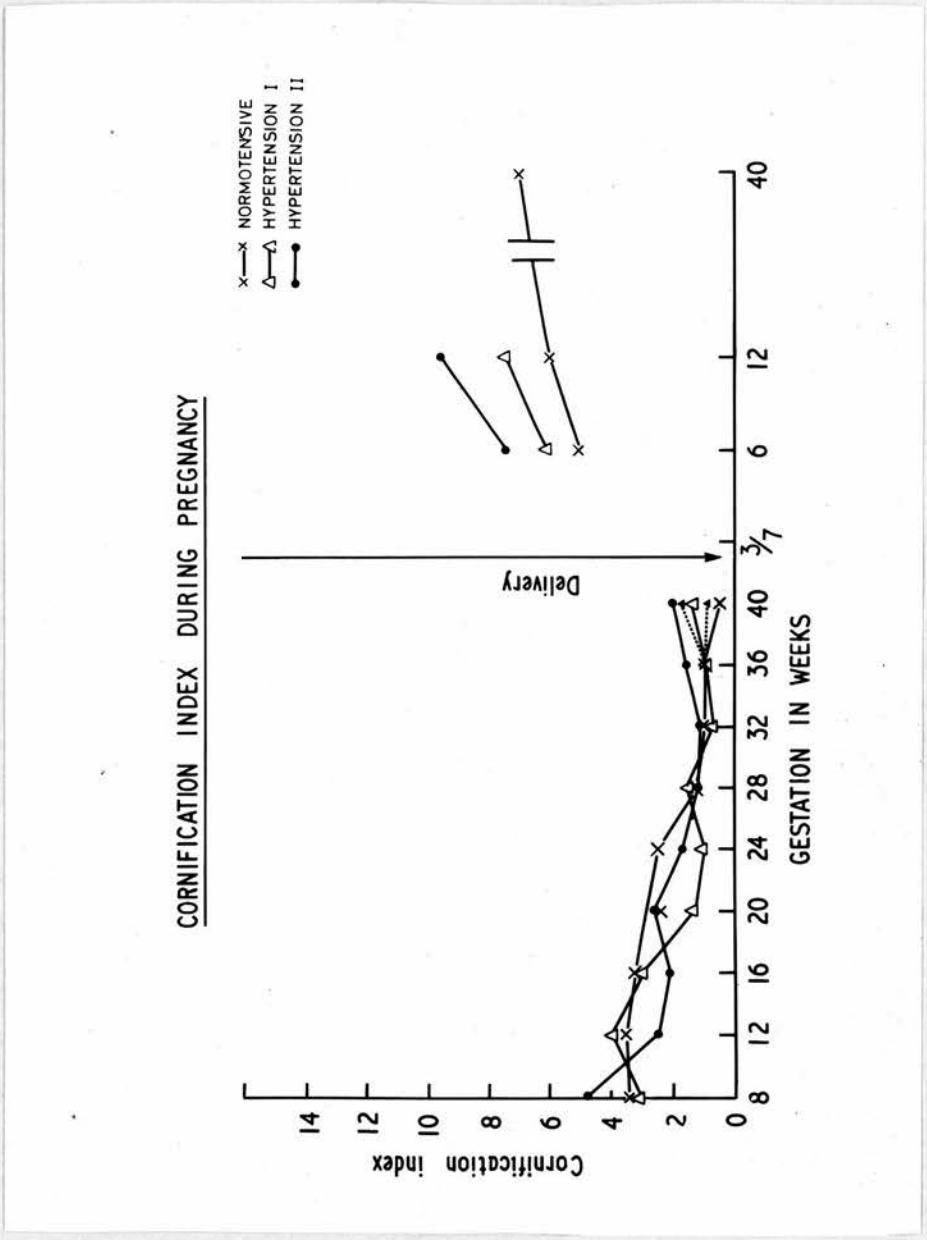



Figure XXVII

The cornification index during pregnancy. The corrected figures are shown by the dotted line and closed triangles.

# DISCUSSION

## DISCUSSION

This is the only study in which fore-arm and hand blood flow rates have been measured in normotensive and hypertensive pregnancy in each subject in each four-weekly interval from 8 weeks gestation to delivery and at increasing intervals to 40 weeks after delivery. It is also the only study which has included detailed analysis of non-pregnant fore-arm and hand flows with regard to reproducibility of results and relationship with various physiological functions. Concurrent studies have been made of physiological factors which may influence the peripheral circulation in pregnancy and an attempt has been made to confirm or refute correlations between these parameters.

Subjects were studied under conditions in which all known factors influencing peripheral circulation were abolished or diminished as far as possible. Where it has not been possible to abolish a variable, control experiments have been made to assess the extent of the possible effects and the results interpreted in the light of these corrections.

Statistically, the only acceptable method of following physiological changes in pregnancy is to measure within patient change. This means that the experiment should be designed to include the same subjects in each interval of pregnancy. Change in the parameter is calculated individually for each subject to obtain the mean change over any chosen interval. This is particularly important when a maximum change occurs at different intervals in each patient. When isolated readings are made at different stages of pregnancy on

different subjects a distorted view can be obtained from a mean curve so obtained because it does not reflect within subject changes and not every subject reveals the maximum change at the same interval in pregnancy.

To make reference easier the rest of the Discussion is presented under the various headings and a Commentary is provided at the end.

The Physiological Basis of Fore-Arm and Hand Flow Rates

Grant et al (1938) using X-rays showed that 85 per cent of the proximal part of the fore-arm consisted of skeletal muscle, the rest being made up of skin and bone. Fore-arm blood flow studies, therefore, measure mainly skeletal muscle flow. Skeletal muscle blood vessels are supplied by sympathetic vaso-constrictor and vaso-dilator fibres. Vaso-constrictor activity in these vessels is reflexly modified by stimulation of receptors in the low pressure vessels in the thorax. Thermo-regulatory reflexes play no part in controlling these responses. The cholinergic vasodilator fibres are activated by emotional stress.

Greenfield et al (1951) showed that the majority of blood through the hand was in the digits because of the arterio-venous anastomoses. Studies of hand flow rate, therefore, measure skin flow mainly. Skin blood vessels are supplied by sympathetic vaso-constrictor fibres and their main action is on the vessels in the distal parts of the limbs. Vaso-motor control in the hand is largely through the release of vaso-constrictor tone. Reflex control of other skin areas is mostly by active vaso-dilatation via sympathetic fibres to the sweat glands. Sympathetic nerves to skin vessels and

and sweat glands are activated by changes in blood temperature acting directly on the temperature regulating centre and by afferent impulses to the centre from skin receptors. Muscle vessels are not involved in the resultant changes in flow.

## Fore-Arm Blood Flow Rates in Pregnancy

### Resume of literature

There have been six studies on fore-arm blood flow rates in pregnancy. All used waterbath plethysmography. Conflicting conclusions have been made from the data obtained. From the details published the differences in conclusions could be accounted for by differing technqques and different experimental design; but in all published reports the paucity of detail make comparisons difficult. In only one study is an acceptable experimental design inferred but the exact figures are not publsshed. An attempt has been made to provide a table summarising the experimental design details (see Table 42 ). Pregnancy has been divided into different intervals by each set of workers and theddefinition of normal pregnancy has seldom been made. Also, in few has specific reference been made to blood pressure levels.

With regard to control non-pregnant levels, in all but one study data was available, but few have investigated the control group for variations with physiological function.

### Results in 'Normal' Pregnancy

No change in the fore-arm blood flow during pregnancy was reported by Abramson et al (1943) and more recently by Ginsburg and Duncan (1967). The former showed no change compared with the non-pregnant control group or with the post-natal readings. The latter

Table 42

## Fore-Arm Flow Rates

| | "Normal Pregnancy" | | | | | | "Hypertension" | | "Pre-Eclampsia" | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Authors | Abramson, Flachs & Fierst | Burt | Herbert, Banner & Wakim | Spetz | Goodrich & Wood | Ginsburg & Duncan | Burt | Ginsburg & Duncan | Burt | Spetz | Ginsburg & Duncan |
| Publication Year | 1943 | 1949 | 1954<br>1958 | 1964 | 1964 | 1967 | 1949 | 1967 | 1949 | 1964 | 1967 |
| Control Group:<br>Mean<br>S.D.<br>No. | 1.5<br>0.5<br>45 | 2.06<br>-<br>6 | 4.56<br>0.10<br>25 | 2.8<br>0.45<br>21 | 3.39<br>0.96<br>20 | None | As Before | | As Before | | |
| Experimental Group:<br>Total number of subjects | 12 | 8 | 58 | 27 | 20 | 50 | 5 | 20 | 7 | 38 | 30 |
| Times each subject examined while pregnant | 2-5 | 1 | ? | 4 | ?1 | ? | 1 | ? | 1 | ? | ? |
| Earliest week in which exam. made in each subject | 17 to 35 | 20 to 41 | 12 to ? | 11 to ? | third trimester only | 8 to ? | 29 to 40 | "Before 24 weeks" to ? | 33 to 38 | 26 to 40 | "Before 24 weeks" to ? |
| No. of intervals during pregnancy | 8 | 6 | ? | 10 | - | 8 | 4 | 3 | 5 | 5 | 3 |
| No of subjects in each interval | 2 to 6 | 1-2 | ? | 6 to 14 | ? | 5 to 28 | 1-2 | 6 to 34 | 1-3 | 3 to 14 | 6 to 36 |

Cont. over

Table 42. cont.

Fore-Arm Flow Rates, cont.

| | "Normal Pregnancy" | | | | | | "Hypertension" | | "Pre-Eclampsia" | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Authors | Abramson, Flachs & Fierst (1943) | Burt (1949) | Herbert, Banner & Wakim (1954 1958) | Spetz (1964) | Goodrich & Wood (1964) | Ginsburg & Duncan (1967) | Burt (1949) | Ginsburg & Duncan (1967) | Burt (1949) | Spetz (1964) | Ginsburg & Duncan (1967) |
| Experimental Group, cont. Time of last post-natal examination | 9 weeks | 10 weeks | 10 weeks | None | None | 24 weeks | 3 weeks | "6 & over" | 13 weeks | None | "6 & over" |
| Water bath temperature | 32°C | ? | ? | 36°C | 32°C | 34°C | ? | 34°C | ? | 36°C | 34°C |
| Room temperature range | 25°-27°C | 15.25°-22.50°C | ? | 22°C | 26°-27°C | 19°-21°C | 15.25°-22.50°C | 19°-21°C | 15.25°-22.50°C | 22°C | 19°-21°C |

Hand Flow Rates

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Control Group: | | | | | | | | | | | |
| Mean | 7.2 | 1.5 | None | None | None | None | None | None | None | None | None |
| S.D. | 3.1 | ? | | | | - | | | | | |
| n. | 45 | 8 | | | | - | | | | | |

Cont. over

Table 42 cont.

Hand Flow Rates, Cont.

| | "Normal Pregnancy" | | | | | | "Hypertension" | | "Pre-Eclampsia" | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Authors | Abramson, Flachs & Fierst (1943) | Burt (1949) | Herbert, Banner & Wakim (1954 1958) | Spetz (1964) | Goodrich & Wood (1964) | Ginsburg & Duncan (1967) | Burt (1949) | Ginsburg & Duncan (1967) | Burt (1949) | Spetz (1964) | Ginsburg & Duncan (1967) |
| Experimental group: | | From graph only | | | | | | | From graph only | | |
| Total number of subjects | 7 | 58 | | 2 | | 58 | | 17 | 7 | | 16 |
| Times each subject examined while pregnant | 1-4 | 1 | | 2 | | ? | | ? | 1 | | ? |
| Earliest week each subject seen | 17-35 | 8 | | 16 | | 8 to ? | | "Before 24 weeks" to ? | 20 to 39 | | "Before 24 weeks" to ? |
| No. of intervals during pregnancy | 8 | 6 | | 2 | | 8 | | 3 | ? | | 3 |
| No. of subjects in each interval | 1-4 | 3-15 | | 2 | | 6-28 | | 6-28 | 1 | | 3-15 |
| Time of last P.N. visit | 9 weeks | 2 weeks | | None | | 24 weeks | | "6 weeks & over" | None | | "6 weeks & over" |
| Water bath temperature | 32°C | ? | | 36°C | | 32°C | | 32°C | ? | | 32°C |
| Room temperature range | 25°-27°C | 17° | | 22°C | | 19°-21°C | | 19°-21°C | 17°C | | 19-21°C |

had no control group but showed no change compared with the post-natal readings. In both of these studies the flow rates were relatively low compared with other studies although the water bath temperatures and room temperatures were different.

An increase in fore-arm blood flow rate was first shown by Burt (1949) who compared a mean flow rate of 3.51 mls./100 mls./minute (calculated from readings obtained from one visit in each subject) in the second half of pregnancy with a control value of 2.06 mls./100 mls./minute from 6 non-pregnant subjects. Herbert et al (1954 and 1958) in a series of recordings made from 12 weeks gestation in 58 subjects described as normal showed that the mean flow rate in early pregnancy was lower than their control value of 4.56 mls./100 mls./minute $\pm$ S.D. 0.10 and that a rise did not occur until after 20 weeks gestation. The highest mean level reached was 8.73 mls./100 mls./minute $\pm$ S.D. 0.48 at 36 - 37 weeks gestation which was highly significantly different from the non-pregnant control mean. They also showed that little change occurred early after delivery but that non-pregnant levels were reached by 6 - 10 weeks after delivery. Unfortunately in neither publication were any more actual figures presented but they do state that no change occurred in their control group with stage in menstrual cycle and stated that "a positive correlation was established between change in pregnancy fore-arm flow rates" and "reported blood volume and cardiac output changes." Further, they state that "no correlation could be established between the pattern of changes in the peripheral circulation and known excretion levels of hormones considered essential to

successful gestation." From this it is presumed that estimations of these parameters were not run concurrently with the peripheral flow studies made by these workers and indeed they do not state that they actually measured anything other than fore-arm blood flow rates by plethysmography and change in skin temperatures. Spetz (1964) also showed an increase in fore-arm flow rates from 2.1 mls. per 100 mls./minute at 11 - 13 weeks gestation to 12.3 mls./ 100 mls. per minute at 38 - 40 weeks gestation. The non-pregnant control value was 2.8 mls./100 mls./minute. No readings were made after delivery. Goodrich and Wood (1964),while studying the effect of oral progestogens, obtained a mean non-pregnant control value of 3.39 mls./100 mls./minute ± S.D. 0.96 and showed that this was significantly lower than a mean flow rate of 4.58 mls./100 mls. per minute ± S.D. 1.83 for 20 subjects in the third trimester of pregnancy.

Results in 'Hypertensive' Pregnancy

As previously stated, few writers have related flow rates to blood pressure in pregnancy which may account in part for the difference in flow rates recorded.

Burt (1949) recorded fore-arm flow rates in five subjects described as 'hypertensive' after 29 weeks gestation and found a mean flow rate for the group of 4.53 mls./100 mls./minute which was higher than that found in the "normal" pregnant subjects. However, Ginsburg and Duncan (1967),examining 20 subjects in whom the diastolic had been recoreded as 90 mm. Hg. and over before 24 weeks gestation, showed no change in flow rates, the actual values of which closely

approximated those of their "normal" pregnant patients.

Results in "Pre-Eclamptic" Pregnancy

Burt (1949) measured fore-arm flow rates in seven subjects said to have "pre-eclampsia". The readings were made once in each subject at varying gestational periods after 32 weeks gestation and gave a mean of 4.47 mls./100 mls./minute. This was not different from her figure for "hypetensive" pregnancy but higher than that for the "normal" group. Spetz (1964) examined 38 subjects with diastolic levels of 90 mm. Hg. and over before treatment after 27 weeks gestation and found an increase in flow rate after this time but to a lesser degree than that shown by his "normotensive" group; the highest level reached was 8.7 mls./100 mls./minute at 38 - 40 weeks gestation. In contrast, Ginsburg and Duncan (1967) examined 30 subjects in late pregnancy who had blood pressures recorded at 90 mm. Hg, or over and showed no change in the flow rates during pregnancy. The figures closely approximated those for their "hypertensive" and "normotensive" groups. They included patients under treatment.

## Comparison of Published Data with the Present Fore-Arm Flow Rate Study

### I - Control Groups

There was a wide range of mean fore-arm blood flow rates in the non-pregnant groups. Abramson et al (1943) obtained a mean of 1.5ml. per 100 mls./minute in 45 subjects and Goodrich and Wood (1964) found a mean of 3.39 mls./100 mls./minute in 20 subjects. In both these groups the water-bath temperature was 32° C. and the room temperature 25 - 27°C. As the differences could not be ascribed to

temperature differences it may be that there was a difference in technique and in particular in the sensitivity of the recording apparatus. Differences in the other published figures may also have been due to temperature effects as well as technique.

The mean fore-arm blood flow rate of the control group in this study is very similar to those of Herbert et al (1954 and 1958) and Goodrich et al (1964), although the relevant temperatures of the former are not recorded and the room temperature of the latter was higher than that in the present study.

1. Age

The effect of age on fore-arm flow rates has only been studied by Hellon et al (1959) who used the strain-gauge technique in 50 male subjects aged from 18 to 73 years. They concluded that fore-arm flow rates increased with increasing age. In the present study the opposite effect was noted. No information is available comparing fore-arm flow rates between males and females but the differences in effect could be due to the fact that both studies selected a relatively small sample of the population and the changes were not measured within subjects but between different subjects of each age.

2. Parity

There is no information on the effect of parity in the control groups of the pregnancy studies although Herbert et al (1954 and 1958) agree that no differences in effect during pregnancy were noted between primiparous amd multiparous subjects.

3. Menstrual Cycle

Similarly, studies at different stages of the menstrual cycle

were carried out only by Herbert et al who found no change, a finding which agrees with this study. Goodrich et al (1964) found an increase in fore-arm flow rate after administration of progestogens with oestrogen derivatives.

4. Blood Pressure

No significant difference was found in this study between fore-arm blood flow rates in the normotensive group and the hypertensive group but the highest blood pressure recorded in the hypertensive group was only 150/95 mm. Hg. Abramson and Fierst (1942) measured fore-arm blood flow rates in 56 normotensive subjects (definition not stated) and 37 hypertensive subjects who had a mean blood pressure of 195/112 mm. Hg., range 150-255 mm. Hg. systolic and 88-162 mm. Hg. diastolic. None of the hypertensive subjects had symptoms. The mean flow rate for the normotensive group was 1.77mls. per 100 mls./minute ± S.D. 0.7 and that for the hypertensive group was 2.86 mls./100 mls./minute ± S.D. 1.2. They say that this is a highly significant difference. They found a positive correlation between increasing flow rates and increasing systolic and diastolic levels. When corrected for age differences the correlation was still significant.

5. Haemoglobin

No correlation was found in this study between haemoglobin level and fore-arm flow rates but none of the subjects were anaemic. Abramson, Fierst and Flachs (1943) found a resting fore-arm flow rate of 1.6 mls./100 mls./minute ± S.D. 0.3 for 25 healthy subjects which was significantly lower than the 2.5 mls./100 mls./minute mean for 11 subjects with haemoglobin levels of 5.1 to 9.6 G.%.

Exceedingly few of our subjects reached these low levels of haemoglobin even in mid-pregnancy so it is doubtful whether anaemia had any effect in increasing the pregnant flow rates.

6. Posture

No studies on change in posture were possible with the apparatus used in this study. Brigden et al (1950) showed that higher forearm flows were found in the supine position than in the upright position in 12 normal subjects lying on a tipping table. No change in systolic pressure was noted during this manoeuvre but significantly lower pulse rates were found in the supine position. However, these studies were carried out over intervals of ten minutes only. The immediate effect of tipping the patient into the upright position is to lower the fore-arm blood flow sharply but over the period of ten minutes the flow rate increases and approaches supine levels at the end of that time. No studies on posture effect in the normal patient have been carried out over periods longer than ten minutes.

II - Pregnancy

1. "Normal Pregnancy"

In the present study the "normotensive" group showed a small but significant rise during pregnancy. Increases in fore-arm flow rates in "normal" pregnancy were shown by Burt (1949), Herbert et al (1954, 1958), Spetz (1964) and Goodrich et al (1964) but the increases were greater than those found in the "normotensive" group in this study. This may be due in part to differences in water-bath and room temperatures but is more likely to be due to the fact that many workers would have included subjects in the Hypertension I group under the heading "normal" pregnancy.

Abramson et al (1943) and Ginsburg et al (1967a) showed no change during "normal" pregnancy and in both series, despite difference in water bath and room temperatures, the readings obtained are low, ranging from 1.5 to 2.5 mls./100 mls./minute in the former group and from 1.9 to 2.7 mls./100 mls./minute in the latter. These ranges are not outside those of the "normotensive" group of the present study. As each patient was not examined in each interval no within patient change could be estimated and may have been obscured by the experimental design. In fact, comparing mean flow rate at 8 - 11 weeks gestation with at 36 - 39 weeks in this study by an unpaired t-test (an unacceptable calculation in the present study as the same patients were present in each interval) there is no significant difference; $t = 1.280$ on 41 degrees of freedom, $0.3 > P > 0.2$. This shows how small but significant changes can be missed by not using a within subject change experimental design. Unfortunately, it cannot be proved that this is the explanation for the findings of Abramson et al and Ginsburg et al. There may have been differences in technique or sensitivity in the recording apparatus.

2. "Hypertensive Pregnancy"

The findings in the Hypertension I group of the present study agree with Burt (1949) and disagree with Ginsburg et al (1967b). Burt did not have readings before 29 weeks gestation to compare the degree of rise but the readings found in the latter part of pregnancy are very similar. Again, definitions of the blood pressure groups vary between the studies and the experimental designs are different. The readings obtained by Ginsburg et al (1967b) are low.

3. "Pre-Eclamptic" Pregnancy

The findings in the Hypertension II group of the present study agree with Burt (1949) in that faster flow rates are attained in this group towards the end of pregnancy compared with "normal" pregnancy. Spetz (1964) also shows an increase in fore-arm flow during pregnancy but not to a higher level than his "normal" pregnant group. Burt did not examine her patients until after 32 weeks gestation and Spetz did not examine his until after 26 weeks gestation so that the degree of increase cannot be measured. Ginsburg et al (1967b) showed no change and once more her readings are the same as those for her "normal" pregnant group. It is difficult to explain why Ginsburg et al show such consistently low flow rates, especially as the water bath temperature was $2^{o}C$. higher than that used in the present study. As the room temperatures were the same and the hand flow rates obtained by Ginsburg et al under the same conditions are low it may be due to insensitivity in the apparatus. Also, some of her patients were being treated.

When interpreting the fore-arm blood flow rates found in this study, it must be remembered that many of the patients were not studied at the time of maximal blood pressure. This was to avoid treatment effect. Also, in the normotensive group the blood pressure at the time of flow showed no change throughout pregnancy. The changes in fore-arm flow rates preceded the changes in blood pressure.

The only subject to be examined ante-natally while an in-patient was in hospital for considerable periods of time due to her twin pregnancy and hypertension. Her case is reported separately. All

post-natal patients were ambulant when examined. Two subjects who were delivered by Caesarean Section were examined on the 7th day after delivery and one of these is reported separately.

4. Correlation with Other Physiological Changes in Pregnancy

Only Herbert et al have commented upon the relationship between change in fore-arm flow rate and other physiological changes in pregnancy (see page 215), but concurrent measurements were not reported; if they were made. They failed to find a correlation between fore-arm flow rates and reported hormone levels. In this study a positive correlation was found between change in fore-arm flow rate and change in pregnanediol excretion and cornification index.

5. Comparison with Non-Pregnant Control Levels

Of the three studies which began early in pregnancy only two had non-pregnant levels available for comparison. Herbert et al state that until 20 weeks gestation the mean fore-arm flow rate was less than the non-pregnant level of 4.56 mls./100 mls./minute. Spetz gives a control value of 2.8 mls./100 mls./minute and a mean of 2.1 mls./100 mls./minute for 11 - 13 weeks gestation. These findings of a decreased flow in early pregnancy compared withnnon-pregnant control levels is confirmed in the present study. After delivery, Herbert et al found that the fore-arm flow rates were the same as those of the control level but Spetz has no post-natal figures for comparison.

6. Abortion; Twin Pregnancy; Latent Diabetes; Placental Insufficiency; and Accidental Ante-Partum Haemorrhage

No literature could be found on peripheral circulation in pregnancy before spontaneous abortion, in patients with placental

insufficiency or accidental ante-partum haemorrhage. Multiple pregnancy was studied after 26 weeks in 14 subjects without hypertension by Duncan and Ginsburg (1968) who found an insignificant increase in limb blood flow rates over the normal range. In this study only one patient with twin pregnancy was examined and her pregnancy was complicated by hypertension, oedema and anaemia; nevertheless, faster flow rates were found. Spetz (1965) studied patients with frank diabetes and found that the increase in fore-arm flow rate occurred earlier in pregnancy than in the normal subject. Similar changes were noted in the only case of latent diabetes examined in this study.

7. The Effect of Posture in Pregnancy

Brigden etal (1950) studied the effect of posture on fore-arm flow in a pregnant subject. In early pregnancy they found no change in fore-arm flow rates when the patient was examined in the supine and lateral positions. In late pregnancy the strict supine position resulted in a fall of auricular pressure and cardiac output, a rise in leg vein pressure and vasoconstriction in the fore-arm. They found that the circulation was restored to normal by turning the patient slightly to one side. These findings have been confirmed for cardiac output by Kerr et al (1964), Kerr (1965 and 1968) and Lees et al (1967b). A rise in fore-arm blood flow was noted in the non-pregnant subject by Roddie et al (1956) when blood trapped in the legs by compression cuffs was suddenly allowed back into the circulation. This is a manoeuvre analagous to removing the uterine obstruction of the inferior vena cava. They state that in these cases the effect rapidly diminishes. As noted before, (see page 220) these changes in

late pregnancy were measured over comparatively short intervals (15 to 20 minutes) and there is no information available about acclimatisation to changes of posture over longer periods of time when it is reasonable to suppose homeostasis might occur. It is known that when supine posture remains constant over two hours and the water bath temperature is maintained at a constant chosen temperature not above 35°C. there is very little change in fore-arm flow rate (Barcroft and Edholm, 1942), but it takes seven to 15 minutes to apply the water bath plethysmograph after assumption of the supine position and this is the time over which studies on change in posture have been made using other techniques. From this it would appear that in the present study, which was carried out in the supine posture throughout pregnancy, fore-arm flow rates would be expected to be constant over the period in which they were measured (40 to 60 minutes after lying down) at least for patients in early pregnancy. If the effect of assuming supine posture in late pregnancy persists for sixty minutes it would render our results in late pregnancy artificially low. Certainly, no significant change in flow rate was noted between 40 and 60 minutes after lying down in late pregnancy. Nothing is known about the effect of posture change on patients with symptomless mild hypertension comparable to that occurring in pregnancy.

## HAND FLOW RATES IN PREGNANCY

Resume of literature (See Table 42)

Only four plethysmographic studies of hand blood flow rates in pregnancy are reported in the literature. All are agreed that there is an increase in flow rate to the hand which increases as pregnancy

advances. Abramson et al (1943) working with a water bath temperature of 32°C. and room temperature of 25-27°C. found a control level of 7.2 mls./100 mls./minute ± S.D. 3.1 in 45 subjects. However, only seven 'normal' pregnant subjects were examined on one to four occasions from 17 weeks onwards. He showed a rise in hand flow from 5.1 mls./100 mls./minute at 17 - 19 weeks gestation to 17.1 mls. per 100 mls./minute at 38 - 40 weeks gestation. Burt (1949) did not report her findings except in graph form, from which only approximate readings can be extrapolated. She did not state the water bath temperature and room temperature was low (17°C.). Her mean non-pregnant level in eight subjects was approximately 1.5 mls./100 mls. per minute and during pregnancy she examined 58 subjects on one occasion at varying stages of pregnancy, beginning at "12 weeks and under" when the flow rate was approximately 2.0 mls./100 mls. per minute. There was a rise in the mean flow rate to approximately 13.5 mls./100 mls./minute at 37-40 weeks gestation but there was an exceedingly wide scatter and a large number of subjects in late pregnancy had flow rates below 5 mls./100 mls./minute. Ginsburg and Duncan (1967) had no control group. They examined 58 subjects during pregnancy. The mean flow rate before 14 weeks gestation was 2.7 mls./100 mls./minute rising to 18.1 mls./100 mls./minute at 39 weeks to delivery. After delivery there was a gradual drop to 4.5 mls./100 mls./minute by 24 weeks. Spetz (1964) reported measurements on two subjects at 16 weeks and 39 weeks gestation and found an increase from 8.5 mls./100 mls./minute to 25.0 mls./100 mls./minute.

In "hypertensive" pregnancy Ginsberg et al (1967b) examined 17 subjects and showdd no significant difference from the "normal" group.

In "pre-eclampsia" Burt examined seven subjects once from approximately 20 weeks gestation. The data was not published and had to be extrapolated from a graph but all except one figure was in excess of her mean for the normal subjects for the appropriate period of gestation and ranged from 14 to 43 mls./100 mls./minute. Ginsburg and Duncan examined 16 subjects at varying times in pre-eclamptic pregnancy and showed no diffeerence between this group and their "normal" pregnant subjects.

Digital Flow Rates

(a) Digital plethysmography has been carried out in serial observations in normal pregnancy by Herbert et al (1954, 1958) who showed increasing flow and increasing vasomotor changes with increasing gestation. Mendlowitz et al (1958) also used digital plethysmographs in the last trimester of pregnancy in 16 "normotensive" and 16 "hypertensive" patients and showed a significant increase over the non-pregnant levels found in 23"normotensive" and 36 "hypertensive" subjects. No difference was found between digital flow rates in normotensive subjects compared with hypertensive subjects either non-pregnant or pregnant. Reflex vasodilatation increased the flow rates in both non-pregnant groups equally. Equal vasodilatation occurred in the pregnant groups but the peak flows did not exceed those of the non-pregnant.

(b) Digital temperature has also been used to assess blood flow rates in pregnancy by Burt (1949) and Herbert et al (1954, 1958). Both showed increasing digital temperature with increasing gestation.

## COMPARISON OF PUBLISHED DATA WITH THE PRESENT HAND FLOW RATE STUDY

### I - The Control Groups

The mean hand flow rate of the control group in the present study agrees with that of Abramson et al (1943). Burt (1949) found a low control group mean but the room temperature was lower in her study. No other control readings are published.

1. Age

No change in hand flow rates with age was found in the present study. Duff (1956) examined hand flow in 36 subjects, mostly men, from 20 years to 50 years and found no change. Similarly, Burt (1949) showed no difference in resting digital temperature with age in her control group.

2. Parity

No change in hand flow rate was found with increasing parity in this study. This confirms the findings of Burt and Herbert et al, who examined digital temperatures.

3. Menstrual Cycle

In the present study a significant decrease was found in hand blood flow measured before and after ovulation in the control group. Burt showed a decrease in digital temperature in the post-ovulatory period but McCausland et al (1961) showed increased digital venous distensibility at this time.

4. Blood Pressure

Abramson and Fierst (1942) examined hand flow rates in 61 normotensive subjects (levels were not defined) and 32 symptomless hypertensive subjects with blood pressure ranging from 150-255 mm. Hg. systolic pressure and 88-162 mm. Hg. diastolic pressure. They found

that the mean hand flow in the normotensive group was 9.32 mls. per 100 mls./minute ± S.D. 2.1 which was significantly faster than the hypertensive group with a mean of 5.38 mls./100 mls./minute ± S.D. 2.2.

The effect of blood pressure on hand flow rates was also studied by Duff (1956). His control group of healthy subjects consisted mainly of men. I have recalculated his findings for women alone. Five of the group were women who had a mean hand flow rate of 5.62 mls. per 100 mls./minute ± S.D. 1.94 which was significantly lower than the 11.34 mls./100 mls./minute ± S.D. 5.2 for the men; $t = 2.409$ on 34 degrees of freedom, $0.05 > P > 0.02$. Seven of the women , with a blood pressure range of 220-250 mm. Hg. systolic and 100-120 mm. Hg. diastolic had a mean hand flow rate of 14.3 mls./100 mls./minute ± S.D. 5.52. This was significantly higher than the normotensive group; $t = 3.334$ on 10 degrees of freedom, $0.01 > P > 0.001$. Nine women had a blood pressure range of 205-290 mm. Hg. systolic and 130-160 mm. Hg. diastolic. The mean hand flow rate was 9.76 mls. per 100 mls./minute ± S.D. 3.99 which was just not significantly greater than the normotensive group; $t = 2.154$ on 12 degrees of freedom, $0.1 > P > 0.05$. There were two subjects with blood pressures of 270/176 mm. Hg. and 250/190 mm. Hg. who had hand flow rates of 2.1 and 2.3 mls./100 mls./minute respectively.

This is reported in detail here as it is the only published report enumerating the data. It is interesting to note that in Duff's series only 5 out of 36 control subjects were women but 18 out of 25 hypertensives were women. Excluding the men from the control group made a substantial decrease in the mean hand flow rate but

excluding the men from the hypertensive group made almost no difference to the mean for each blood pressure group. This had the effect of exaggerating Duff's original conclusions.

Mendlowitz et al found no difference in digital flow in normotensives and hypertensive control subjects.

In this study no significant difference was found in the control group between patients with blood pressures of 120/80 mm. Hg. and under and those with blood pressures over 120/80 mm. Hg. There were small numbers in the groups and none had a blood pressure of over 150/90 mm. Hg.

5. Haemoglobin

Abramson, Fierst and Flachs (1943) measured hand flow in non-anaemic subjects and in those whose haemoglobin levels ranged from 5.1 - 9.6 G.% and found a decrease in hand flow rate from 8.1 mls. per 100 mls./minute ± S.D. 3.5 for the control group to 6.3 mls. per 100 mls./minute for the anaemic group which was not significant. None of the subjects in this study had such low haemoglobin levels.

6. Smoking

The effect of smoking on hand flow rates was examined by Shepherd (1951) who found a transient effect during smoking at the subjects "normal" rates, but no difference between the "before" and "after" mean flow rates. The findings in this study are in agreement.

Pregnancy

All studies on hand and digital blood flow are agreed that there is an increase in blood flow rate with increasing gestation.

Ginsburg et al could find no difference in "hypertensive" or "pre-eclamptic" pregnancy. Mendlowitz et al found no difference

in digital flows in normotensive and hypertensive pregnancy. This study can neither support nor refute the findings in hypertensive pregnancy as only three of the subjects were normotensive but there is a suggestion that there may be a difference as the mean maximum increase in hand flow rate in the three normotensive subjects was 11.5 mls./100 mls./minute and for the hypertension I group it was 20.0 mls./100 mls./minute. However, when correlation between change in hand blood flow and change in blood pressure was tested for all subjects there was no significant result.

## BLOOD PRESSURE IN PREGNANCY

### 1. Blood Pressure in Normal Pregnancy

Cohen etaal (1939) studying patients in whom the blood pressure was alsays under 140/90 mm. Hg. showed an average slight decrease in blood pressure with advancing pregnancy followed by a slight rise towards term. They noted an increase in pulse pressure with advancing pregnancy. Burwell (1938) also noted a slight decrease during pregnancy, more marked in the diastolic level than the systolic, resulting in an increase in pulse pressure. Andros (1945) studied the blood pressure throughout pregnancy in 300 private patients with pre-pregnancy records. Each patient had blood pressure measured at least 11 times during pregnancy. He excluded patients with readings of 140/90 and over. The within patient change was estimated. There was no change in the systolic pressure throughout pregnancy and no change compared with the non-pregnant levels. The diastolic level in the first three months of pregnancy was on average 3.48 mm. Hg. lower than the pre-pregnancy levels. No further change occurred until the last three months when the diastolic pressure rose to pre-pregnancy levels. The highest mean systolic level in

pregnancy was 115.17 mm. Hg. and highest mean diastolic level was 71.97 mm. Hg. These levels and changes are in agreement with the present findings in the normotensive group; namely that there is no mid-trimester drop and a small significant rise occurs towards term. However, Walters (1966) found a mid-trimester drop in diastolic in his 30 patients studied at rest while estimating cardiac output. The actual range of levels agrees with the present study.

2. Blood Pressure in Complicated Pregnancy

The largest study on blood pressure was made in Aberdeen from records of 4,215 primigravidae attending the normal Antenatal Clinic from before 20 weeks gestation (McGillivray, 1961). Conditions were not, therefore, standardised but it is very interesting to note the correlation between blood pressure changes found and the incidence of complications of pregnancy. When levels of 80 mm. Hg. diastolic pressure and 130 mm. Hg. systolic pressure are reached and exceeded by 20 weeks gestation there is an increased incidence of albuminuria later in pregnancy. A rise of 5 mm. Hg. or more diastolic pressure or a rise of 10 mm. Hg. or more systolic pressure from 20 to 30 weeks gestation was significantly related to incidence of albuminuria and perinatal loss. These findings add weight to the rationale of dividing the subjects in the present study into blood pressure groups based on 120/80 mm. Hg. and not the standard 140/90 mm. Hg. Validity of such a division is also emphasised by the significantly different findings in peripheral circulatory changes.

Although many of the significant differences are present in this study because of the experimental design, several facts emerge which are not inherent.

In the first instance no mid-trimester drop was demonstrable, although there was a steady slight decline in blood pressure between intervals in the control group. Secondly, compared with the normotensive group, a significant rise in systolic pressure occurred at 16 - 19 weeks gestation in the Hypertension II group and this rise preceded the significant rise in diastolic pressure by two to three intervals. Thirdly, the amount of change in the highest blood pressure recorded in each interval in pregnancy did not differ significantly between the normotensive and Hypertension I groups and in both these groups the blood pressure had returned to the respective first visit levels by 12 weeks after delivery, whereas there was still a significant increase in pressure in the Hypertension II group at this time. By nine months after delivery all groups had returned to their respective first visit levels, the Hypertension I group remaining significantly higher than the normotensive group.

## FORE-ARM PERIPHERAL RESISTANCE UNITS.

These units are a direct reflection of the accuracy of measurement of the blood flow rate and the conditions under which these measurements are made as the technique for measuring blood pressure is better standardised than techniques for measuring blood flow.

It is these differences in flow rates which account for the differences in peripheral resistance units found by various workers studying pregnancy. In this study the general trend of a fall in peripheral resistance units during normotensive pregnancy confirms the findings of Spetz (1964). He finds a much greater decrease

because he found higher fore-arm flow rates with increasing gestation, (see Discussion on Fore-Arm Flow Rates). Similarly, because he found slightly lower fore-arm flow rates in the pre-eclampsia group he finds an increase in peripheral resistance units compared with the normotensive group. As blood pressure tends to show a slight rise towards term and Ginsburg et al found no change in fore-arm flow rates they demonstrated an increase in peripheral resistance with increasing gestation which was more marked in the hypertension groups but owing to the experimental design no within patient changes can be elicited from the published data.

## PULSE RATE IN PREGNANCY

In the present study the pulse rate was already significantly raised at 8 - 11 weeks gestation in comparison with the post-natal levels and the non-pregnant group. This confirms the findings of Cohen et al (1936), Hamilton (1949), Brehm et al (1955), Dahlstrom et al (1960), Walters (1966) and Roy et al (1966). Thereafter, a small but insignificant rise occurred in this study confirming the findings of Cohen et al (1936), Hamilton (1949), Werko (1954) and Walters (1966) and Roy et al (1966). Burnell (1938) and Brehm et al (1955) found a further rise with increasing gestation. All agree that the pulse rate drops to non-pregnant levels early in the puerperium.

## ORAL TEMPERATURE IN PREGNANCY

In early pregnancy body temperature was significantly higher than the non-pregnant control group and decreased steadily and

significantly throughout pregnancy reaching non-pregnant levels near term. Comparing the body temperature at 8 - 11 weeks gestation with that 12 weeks after delivery within patients showed that in early pregnancy the temperature was, on average, 0.81°F ± S.D. 1.0 higher. It is well known that the post-ovulatory increase in basal body temperature is sustained after the first missed period (e.g. Davis, 1946). Buxton et al (1948) studying patients during pregnancy found that in early pregnancy the basal body temperature was between 0.5 and 1.0°F. greater than the non-pregnant level and that this was maintained until mid-pregnancy after which there was a decline to non-pregnant levels by term. They found that progesterone given to patients with amenorrhoea produced a rise in body temperature whereas oestrogen produced a slight depression of temperature. If the ovaries were present they showed that giving chorionic gonadotrophin maintained the pregnanediol induced increase in temperature. Kappas et al (1961) described the pyrogenic effect of various steroids and their excretion products and in particular found that etiocholanolone and pregnanediol breakdown products of progesterone produced a rise in body temperature. Kaiser (1955) infers that the fall in body temperature late in pregnancy was probably due to oestrogens. The effect of progesterone on body temperature was greater than that of oestrogen (Buxton et al, 1948). This is confirmed by the fact that the body temperature is highest in early pregnancy when pregnanediol excretion is rising slowly but oestriol excretion is increasing rapidly (Klopper et al, 1963). Also, Buxton et al found human chorionic gonadotrophin to sustain the rise in temperature due to pregnanediol and the serum levels of this hormone

are highest from 8 - 15 weeks gestation (Michele etal, 1963; MacGregor et al, 1966). In mid-pregnancy pregnanediol excretion increases rapidly while there is a diminution in the rate of excretion of oestriol but the body temperature continues to fall. This may be due to the fact that serum human chorionic gonadotrophin levels have fallen very sharply. In late pregnancy the rate of increase in excretion of pregnanediol decreases while that of oestiol again increases rapidly. At this stage, it may be that oestrogen has its most marked effect as human chorionic gonadotrophin levels remain lowered and the body temperature continues to fall.

## THE BLOOD VOLUME IN PREGNANCY

### Resume of Literature and Comparison with the Results in this Study

### I - The Control Levels

1. Sex

Gibson and Evans (1937) and Crooke and Morris (1942) noted that women had significantly lower blood volumes than men after correction for height and weight.

2. Age

The former workers noted that in early and middle life blood volumes were the same but there was a decline after middle age. Thus age of the patient in the pregnancy studies would not influence the results.

3. Height, weight and surface area

Gibson and Evans also confirmed the findings of Rowntree et al (1929) that blood volume was related to surface area and height and less to weight. Roscoe et al (1946) and Hytten et al (1963) found similar correlations and these were confirmed in the present study.

4. Blood Pressure

Eisenberg et al (1965) examined blood volumes in normotensive and hypertensive subjects and found no difference when the subjects were supine. When the same patients were studied standing up there was a significant fall in blood volume in both groups but a much greater fall in the hypertensive group. In this study the effect of posture was not examined but in the supine position no difference was found between the normotensive and hypertensive subjects in the late post-partum period.

5. Heart Size

In the non-pregnant Kjellberg et al (1950) noted a correlation between blood volume and heart size.

II - The Blood Volume in Pregnancy

Numerous studies on blood volume in pregnancy have been made since 1934. All have used different experimental designs; some have used different patients at different intervals in pregnancy, some have used the same patients at different intervals. Selection of patients as "normal" also differs; most have used Evans Blue Dye but different methods of administration and extraction have been used. Some have made corrections for trapped plasma, some for body surface area or weight. However, they all agree that the mean blood or plasma volume increases during pregnancy although there is a wide individual variation between subjects and the maximum levels are reached at different times during pregnancy. An effort has been made to provide a brief summary in the Table 43 . There is agreement that the blood volume ceases to increase as term approaches.

Table 43

Summary of Published Data on Blood Volume Changes in Pregnancy

| Authority | Year | Method | Serial or Cross Sectional Study | Mean Total Increase % | Slight Fall at Term | Note |
|---|---|---|---|---|---|---|
| Dieckmann et al. | 1934 | Congo Red | S. | 23.0% | - | Wide individual variation, i.e. -1% to +106%, An increase in first trimester of 16% |
| Thomson et al. | 1938 | E.B. | S. | 45 - 65% | Yes | |
| Burwell | 1938 | E.B. | S. | 42.0% | - | Last 6 months pregnancy only. |
| Cohen et al. | 1939 | | | | Yes | No details. Increase to 9 months and slight decrease to term. |
| Roscoe et al. | 1946b | E.B. | S. | 25.6% | - | |
| Brown et al. | 1947 | E.B. | S. | | - | Studies in labour. |
| McLennan et al. | 1948 | E.B. | C. | 32.0% | Yes | None before 35 weeks. |
| Tysoe et al. | 1950 | E.B. | S. | 34.8% | Yes | Notes variability in patients. |
| White | 1950 | E.B. | C. | 23.0% | No | Rise less in pre-eclampsia. |
| Kjellberg et al. | 1950 | C.O. | S. | 42.0% | Yes | |
| Caton et al. | 1951 | E.B. | S. | 45.0% | Yes | |
| Bucht | 1951 | E.B. | C. | 25.7% | - | Plasma volume. |
| Gemzell et al. | 1954 | C.O. | S. | 30.0% | Yes | |
| Adams | 1954 | E.B. | C. | 21.6% | Yes | Plasma volume. |
| Verel et al. | 1956 | E.B. + Cr. | C. | Increased | | Last trimester only. |
| Cope | 1958 | E.B. | S. | 38 - 39% | Yes | Plasma volume. |
| Cope | 1961 | E.B. | S. | | - | After 24 weeks. Increase is less in pre-eclampsia. |
| Paintin | 1962 | E.B. + Cr. | S. | 29.7% | Yes | Plasma volume. |
| Hytten et al. | 1963 | E.B. | S. | 38 - 69% | Yes | Plasma volume. |
| Hytten et al. | 1963 | E.B. | S. | | - | No difference between normotensive pregnancy and pre-eclampsia. |

E.B. = Evans Blue Dye. Cr. = Radio-active Chromium. C.O. = Carbon monoxide method.
S = Serial Study. C. = Cross-Sectional Study.

Other Factors said to affect Blood Volume

1. Parity

The effect of parity on blood volume change in pregnancy has been noted by Dieckmann et al (1934), McLennon et al (1948), Kjellberg et al (1950) and Adams (1954) who agree that there is a greater increase in multiparous pregnancy than primigarous pregnancy. In this study no such effect could be found.

It has been noted already that subjects reach maximum blood volume at varying stages in pregnancy and in the present study every patient was examined at four weekly intervals. A more exact estimate of maximum increase could therefore be obtained than when patients are examined at varying intervals during pregnancy. Also, the maximum change for each patient was calculated separately before obtaining the mean change and was not made in comparison with a separate control group. The mean maximum change in pregnancy for the primiparous group was slightly but insignificantly lower than the multiparous group.

2. Height, weight, surface area, birthweight

Hytten et al (1963) found a positive correlation between increase in plasma volume and maternal stature and birthweight. Their study was carried out on primigravid patients only. No similar correlations could be found in this study. Hytten's estimate of maximum plasma volume increase must be a little more inaccurate than this study, as large numbers of readings are missing from his experimental design, especially in the intervals 25 - 28 and 33 - 36 weeks when only 10 and 8 subjects respectively were examined out of a total of 39 subjects. Two-thirds of our patients attained their maximum level in the period 24 - 35 weeks gestation.

3. Hormone Excretion

Cope (1952) suggested that women secreting more progesterone had greater plasma volumes on the evidence that in prolonged pregnancy the average plasma volume was greater at term than for patients delivered between 38 and 39 weeks gestation. In the present study no correlation was found between increase in blood volume and increase in progesterone levels for the same patients.

4. Rate of Blood Flow

Gibson and Evans found no relationship between blood volume and circulation times in the non-pregnant. No relationship was found between change in blood volume and change in fore-arm flow rates in this study.

5. Blood Pressure

White (1950) and Cope (1961) found the blood volume increased significantly less in pre-eclamptic pregnancy than in normotensive pregnancy. Hytten et al (1963) found no difference in change in plasma volume between 86 normotensive and 23 subjects who had blood pressures of 140/90 mm. Hg. and over in late pregnancy. In this study when maximum change in blood volume was examined there was no significant difference between the blood pressure groups.

6. Heart Size

Both Kjellberg et al (1950) and Hytten et al (1963) failed to find any relationship between change in blood volume and change in heart size measured radiographically.

7. Labour and Puerperium

Brown et al (1947) and Verel et al (1956) studied blood volume changes before and after labour. Both showed significant decreases

in blood volume after delivery. Brown et al found a further significant decrease on the second day after delivery but that it had not reached non-pregnant levels. The findings of the present study confirm that by the third day after delivery a significant drop had occurred but that the blood volume was still significantly higher than in the non-pregnant state. Brown et al (1947), McLennan et al (1948) and Tysoe et al (1950) agree that non-pregnant levels are reached by one week after delivery. Other workers examined their patients for the first time after delivery later than one week and most found non-pregnant control levels. The present study shows that no further change in blood volume occurs from 6 weeks to 40 weeks after delivery.

8. Other

The circulatory changes in pregnancy have often been likened to those due to the presence of an arterio-venous fistula, notably by Burwell (1938) and McGaughey (1952). Warren et al (1951) measured blood volume before and after removal of arterio-venous fistula in 41 subjects and found no change in blood volume in 23 patients, of the rest the decrease was small in most but greatest decrease was 1,060 mls./metre$^2$ surface area. They concluded that, in general, patients with elevated blood volumes had the largest fistula. More recently, Werko (1954), Winner (1965) and Walters et al (1966) have rejected the arterio-venous fistula theory.

## HAEMATOLOGICAL CHANGES IN PREGNANCY

### I - The Haemoglobin and Packed Cell Volume

From a study of the literature there are three main patterns of

change in haemoglobin and packed cell volume during pregnancy. Some haemoglobin levels were estimated by finger-prick at routine antenatal clinics and others by intravenous sampling under controlled conditions, usually while other investigations were being carried out. Packed cell volumes were also measured differently. Not all workers state whether iron prophylaxis was given or not. The nutritional state of the population sampled would also effect the results. Briefly, the earlier workers, Dieckmann et al (1934), Cohen et al (1936), Cope (1958) and Gemzell (1954) showed a steady fall during pregnancy with a slight rise towards term. Roscoe et al (1946) Paintin (1962 and 1963) showed a steady fall with no rise towards term. Lister (1962) and Walters (1966),in serial studies, showed a fall from early pregnancy, the lowest levels being reached at 24 weeks gestation followed by a gradual increase towards term when levels were attained which approximated those found in early pregnancy. The findings in the present study confirm the latter quadratic distribution. Lister does not state whether her subjects were given iron prophylaxis but as the results are very like those of Walters and the present study it is probable that they were. It is interesting to note that despite iron prophylaxis a significant fall in haemoglobin level does occur and reaches minimum value before the maximum blood volume is reached. Also, the haemoglobin level continues to rise at a time when there is no significant change in the blood volume.

II - <u>The Red Cell Count</u>

Dieckmann et al and Gemzell et al found that the red cell count followed the same pattern as their findings in haemoglobin and

packed cell volume. Roscoe et al (1946) and Paintin (1962) showed a decrease to mid-pregnancy and no change in the last trimester. From the blood volume and radio-active chromium studies Paintin calculated an overall increase in total red cells during pregnancy of 9 per cent, reaching maximum levels at 37 weeks in 14 subjects whilst in six subjects the total red cells decreased.

In this study the red cell count followed the same quadratic distribution as the haemoglobin level. From this it follows that there was a relatively greater increase in total red cells later in pregnancy than found by Paintin because the blood volume patterns in the two studies were the same. An overall increase of 20 per cent was found. Caton et al (1951) found an increase in total red cells of 40 per cent in pregnancy, normal levels being reached 60 days after delivery.

III - Mean Corpuscular Haemoglobin Concentration

No significant change in mean corpuscular haemoglobin concentration was found by Roscoe et al (1946), Tysoe et al (1950), Paintin (1962), Walters (1966) or in this study.

IV - The Mean Cell Volume and Mean Cell Haemoglobin

In this study both showed a slight but significant increase which was also demonstrated by the non-pregnant group over six months. It is difficult to explain this. It was not a response to iron prophylaxis as the non-pregnant group did not receive iron. It is unlikely that studies on all the subjects were begun at the same phase of red cell production by chance. Also, subjects were added to the study at different months and different years. More probably

it is a reflection of the inaccuracies of the red cell count as this is used to compute both parameters. In the non-pregnant group there was no change in haemoglobin or packed cell volume over six weeks but there was a slight decrease in the red cell count which was just not significant, $0.1 > P > 0.05$. Perhaps this accounts for the effects in the non-pregnant group and yet the standard deviations for the between interval changes in the pregnant red cell counts were constant.

Roscoe et al and Tysoe et al found no change in mean cell volume and mean cell haemoglobin during pregnancy. Dieckmann et al showed an increase of 20 per cent in the mean cell volume.

V - The White Cell Count

In this study the white cell count was already significantly raised by 8 - 11 weeks gestation compared with the non-pregnant control level and the late post-partum readings. A further significant increase occurred during pregnancy but the mean level never exceeded that of the range of normality quoted by Davidson (1966). On the third day after delivery the highest value was recorded,no doubt stimulated by the presence of an involuting uterus. By six weeks after delivery the white cell count reached normal non-pregnant levels.

## OTHER CIRCULATORY CHANGES IN PREGNANCY

Burwell et al (1938), Palmer et al (1949), Hamilton (1949 and 1950), Bader et al (1955), Werko et al (1950), Adams (1954), Kerr (1965 and 1968), Walters (1966), Roy et al (1966) and Lees et al (1967a and b) all agree that the cardiac output is increased during pregnancy. There is much individual variation and the earlier

studies showed the maximum cardiac output in mid-pregnancy. More recently, it has been shown in serial studies that cardiac output is already raised in the first trimester to levels which are not exceeded later (Walters, 1966; Kerr, 1965; and Lees et al,L967a and b). Walters showed a decrease in cardiac output towards term. Kerr attributes this to the assumption of the supine posture in pregnancy and showed, in association with Lees, in serial studies on patients in the lateral position that no change occurred in cardiac output throughout pregnancy following the first trimester increase.

Studies on the circulation time in pregnancy give conflicting results. Greenstein et al (1937) in a serial study found a gradual increase in arm-tongue and arm-lung times from 18 weeks gestation and a slight fall after 38 weeks. Manchester et al (1946) found that both parameters fell from early to late pregnancy whereas Cohen et al (1936) found a small fall in arm-carotid time to 21 weeks gestation after which the time increased to non-pregnant levels at term.

Fore-arm and hand blood flows have been discussed already. Calf blood flow rates have been measured by Abramson et al (1943) and Ginsburg et al (1967), who showed no change throughout pregnancy; and by Herbert et al (1945 and 1958) and Goodrich et al (1964) who found an increase in late pregnancy. Abramson et al did not measure flows until after17 weeks gestation by which time the pregnant readings did not differ from the control non-pregnant group. Ginsburg et al had no control group for comparison; Goodrich et al did not measure flows in pregnancy antil after 26 weeks gestation. Herbert et al showed that there was a decrease in calf flow in early

pregnancy when compared with the control group; an effect which resembles that found in fore-arm flow rates. Wright et al (1950) showed a decrease with advancing pregnancy in radio-active sodium clearance rates from the dorsum of the foot to the groin. Blood flow rates in the foot have been measured by Ginsburg et al (1967) who found an increase with advancing pregnancy. Toe temperatures also increased as pregnancy advanced according to Herbert et al. The only study on the lower extremities in hypertension and pre-eclampsia was made by Ginsburg et al who found no difference from their normotensive group.

Uterine blood flow rates have been measured in early pregnancy by Assali et al (1953 and 1960). Using electro-magnetic flow-meters they found a rate of 51.7 mls./minute at 10 weeks gestation rising to 185 mls./minute at 28 weeks gestation. Metcalfe et al (1953 and 1955) and Romney et al (1955), using a method based on the Fick principle, found a wide scatter of flow rates at term, the range being 175 to 840 mls./minute and the mean 492 mls./minute. Huckabee (1962) found a range of 700 - 800 mls./minute at term.

Browne et al (1953), Morris et al (1956), Johnson et al (1957) Moore et al (1957) and Dixon et al (1963) found myometrial radio-active sodium clearance and choriodecidual space clearance times to be increased during pregnancy in proportion to the degree of severity of hypertension. Johnson and Clayton found that the effect in hypertension could be reversed by giving a sympatholytic agent but Dixon et al could find no improvement in clearance rates after administration of hypotensive agents. Budenell et al (1961, however, found no difference in clearance rates between normotensive, pre-eclamptic or diabetic patients.

The atherosclerotic and arteriosclerotic changes in the spiral arterioles in the placental bed in hypertensive and pre-eclamptic pregnancy are mentioned elsewhere (page 250). Vessels may be obliterated in severe cases.

Little is known about blood supply to other regions in pregnancy. McCall (1949) found no change in cerebral blood flow in either normotensive or hypertensive pregnancy. Munnel et al (1947) found no change in liver blood flow rates. Sims et al (1958) found high renal flow rates in early pregnancy, levels which were maintained until term approached when there was a decrease towards non-pregnant levels. This fall near term has been described also by Chessley et al (1946) and Bucht (1951). Recently, Chessley et al (1964) and Kerr (1968) have thrown doubt on the decrease on the grounds of supine postural effect. Chessley et al showed no excessive decrease in renal flow in hypertension in late pregnancy unless the patient had previous renal damage, although Goldring et al (1941) showed decreased renal blood flow in non-pregnant subjects with hypertension in the absence of known renal damage.

In summary, early pregnancy is characterised by a significant rise in pulse rate, cardiac output, uterine, renal and breast blood flow and a decrease in venous tone while the blood pressure, hand and foot flow rates remain unaltered, the fore-arm and calf flow rates are decreased and the blood volume shows a slight increase. As pregnancy advances in the normotensive the cardiac output and blood pressure remain the same or show a slight decline; the pulse rate, fore-arm and calf flow rates remain the same or show a slight increase; breast, hand, foot and uterine flow rates and blood volume increase markedly, the venous tone, haemoglobin, packed cell volume

and red cell count decrease rapidly and renal blood flow remains unaltered. Towards term there may be a slight decrease in cardiac output, renal blood flow and blood volume while uterine, breast, hand and foot flows cease to rise so rapidly, venous tone is lowest, fore-arm and calf flows increase, haemoglobin and packed cell volume approach non-pregnant levels, the blood pressure may show a slight increase and pulse rate remains unaltered.

## HORMONE EFFECTS IN PREGNANCY

### I - Pregnanediol Excretion in Pregnancy

The findings in this study closely approximate the published figures, e.g. Shearman, (1959) and Klopper et al (1963) and MacRae (1964). Shearman states that in patients developing hypertension in late pregnancy the pregnanediol excretion is significantly below the mean value for normotensive pregnancy. Booth et al (1965) find similar effects in pre-eclampsia and essential hypertension but state that the levels are in the low part of the normal range. This finding fits in with the fact that the changes in fore-arm flow rate in hypertensive pregnancy were associated with decreasing change in pregnanediol levels during pregnancy. Greig et al (1962) and Russell (1965) note low pregnanediol excretion in unsuccessful pregnancies. Assays were not carried out in the four patients who aborted, or the patient with placental insufficiency leading to intra-uterine death but it is reasonable to assume that they would have shown small increases in pregnanediol excretion. Fore-arm blood flow rates within the hypertensive ranges were found in these normotensive patients.

### II - Cornification Index in Pregnancy

The general trend noted in this series agreed with that found by

MacRae et al (1964). From oestriol and pregnanediol excretion studies they found that there was a good correlation with vaginal cytology in normal pregnancy. In pre-eclampsia and hypertension they noted that vaginal cytology did not reflect the changes in hormone excretion. However, in this study, when within patient trends were measured, it was found that there was a small but significant correlation between small changes in cornification index and large increases in fore-arm flow rate which in turn were related to the degree of rise of diastolic levels. MacRae et al claim that vaginal cytology may reflect poor foetal growth when urinary hormone excretion is within normal limits and Grieg et al (1962) showed that comparison between plasma progesterone levels and pregnanediol excretion in the same patients did not show an exact correlation. They found that plasma progesterone levels during pregnancy were far better reflected by oestriol excretion. This may account for the discrepancies in relationship between vaginal cytology and urinary hormone excretions in some abnormal pregnancies.

III - Summary of Hormone Effects and Vascular Changes

Much of the evidence that oestrogen and progesterone affect the circulation is inferred from clinical observations. For example, there is a lower incidence of atherosclerotic disease in women during the reproductive phase than in men of the same age group. Also, during pregnancy women have warmer extremities than in the non-pregnant state; varicosities become apparent and pre-existing varicosities become worse; vascular spiders and palmar erythema develop and nasal congestion causes snoring.

The investigation of hormone effect on blood vessels is mainly directed towards lipid metabolism (Pincus, 1959; Katz et al, 1963) and atherosclerosis, although Katz et al have noted that oestrogens stimulate growth of collagen and fibroblasts in the vessel wall. Eder (1959) showed that oestrogen reduced an already raised serum cholesterol but other workers (Pincus, 1959) found no effect in reduction of mortality when oestrogens were given to subjects with already diseased vessels. Dixon et al (1958) and Brosens (1964) have shown atherosclerosis and arteriosclerosis in the spiral arteries of the placental bed in patients with hypertension when hormone production is lower than in normal pregnancy. It is difficult to explain why these vessels are so highly susceptible unless it is because they are so close to the site metabolism of the hormones.

Reynolds et al (1939) described the incidence of vascular spiders and palmar erythema in men given oestrogens. The same changes in pregnant woman were noted by Logfren (1942) who endeavoured to reproduce the effect by administration of oestrogen to a woman four months after delivery. He found that palmar erythema recurred but was not so intense as that during pregnancy. Bean (1945) and Bean et al (1947 and 1949) found a significant increase in arterial spiders early in pregnancy and noted a further increase with advancing gestation. They found that by the end of pregnancy 65 per cent of the white patients had vascular spiders and 58 per cent had palmar erythema and that the effects rapidly diminished after delivery and had completely disappeared in most patients by six weeks after delivery. They suggested that the vascular changes were due to oestrogen or a related endocrine substance, perhaps of adrenal origin.

As similar changes are found in chronic hepatic cirrhosis Bean et al (1949) carried out a series of liver function tests on his patients and found no significant change during pregnancy, concluding that the vascular lesions were not due to liver dysfunction. They found no relationship between the incidence of vascular changes and hypertension or pre-eclampsia. Crawford (1950) also described increasing incidence of vascular spiders and palmar erythema with advancing pregnancy. Rose (1949) describes three cases of haemangiomata occurring in pregnancy with regression after delivery.

Reynolds (1940 and 1963) states that oestrogen administration produces no change in blood pressure or heart rate but produced a decrease in venous pressure in the hand in some patients and dilatation of nail bed capillaries. There was, however, no increase in blood flow through the hand and no increase in skin temperature from which he concluded that the vasodilating action was on the smallest capillaries and venules alone and presumed that the mechanism produced a shift of blood to skin for heat loss purposes. He confirmed this by observing blood vessels in the pinna of the rabbit,, but thought that the effect may be an indirect one associated with an increase in acetylcholine in the tissues because the effect was inhibited by atropine. In further experiments, with rabbits, he showed that there was a considerable increase in acetylcholine content of the uterus coincident with a pronounced vasodilatation within an hour of administration of oestrogens. In other experiments he showed an increase in congestion of nasal mucosa after oestrogens had been given. Reynolds also noted that oestrogens caused increased

reticulo-endothelial activity. Later, Sheehan et al (1948) found that at post-mortem, women in the second half of pregnancy had larger spleens than in the non-pregnant state and noted an increased number of cases of ruptured splenic aneurysm during pregnancy.

Uterine arteries increase in length and diameter during pregnancy. Fernstrom (1955) showed, by arteriographic studies, that the enlargement begins early in pregnancy and increases with increasing gestation. Borell et al (1953) showed that administration of oestrogens to women with secondary amenorrhoea increased the width of the uterine arteries. Observation of arteriographs for placental localisation purposes shows that the uterine arteries are the largest on the side of the placental implantation.

From the fore-going evidence it appears that oestrogen has a vasodilatory effect onccapillaries and venules in areas responsible for body temperature regulation as well as on splenic and uterine vessels.

Significant disability due to varicosities can occur early in pregnancy when hormone levels have already risen and the mechanical effect of the enlarging uterus is minimal. It is said to be due to the smooth muscle relaxant effect of progesterone, and its derivatives, on the vessel-wall (Carey, 1963). McCausland et al (1961) found an increase in digital venous distensibility in the luteal phase of the menstrual cycle as well as in pregnancy. Goodrich et al (1964) showed loss of venous tone in fore-arm and calf during pregnancy and during admini tration of oral progestogens with oestrogen derivatives demonstrating that factors other than mechanical were responsible for

the venous distensibility. The latter workers found an increase in fore-arm and calf blood flows also but this finding was not reproduced in the normal menstrual cycles examined by Herbert et al (1954 and 1958) and in this study.

COMMENTARY

## COMMENTARY

A correlation between change in fore-arm blood flow rates and change in diastolic pressure has been demonstrated during pregnancy. It confirms the findings of Abramson et al in the non-pregnant subject although, in pregnancy, there are other factors which might modify the effect. For example, the supine position may have masked a larger increase in fore-arm flow rates in late pregnancy; but, this has not been proved (see page 224). The correlation between change in fore-arm blood flow and change in hormone function is compatible with the known changes in hormone function in hypertensive and pre-eclamptic pregnancy.

If the cardiac output and blood pressure remain the same (Lees et al 1967) increased progesterone activity should produce increased peripheral flow due to decreased peripheral resistance. In normotensive pregnancy the fore-arm blood flow rate does increase significantly while the peripheral resistance falls. However, the greatest increase in fore-arm flow rate is found in hypertensive pregnancy, the rise being proportional to the degree of rise of the diastolic level, and poorer progesterone excretion occurs in these cases. Fore-arm peripheral resistance did not increase in hypertensive pregnancy. Hamilton (1949 and 1950) showed no difference in cardiac output between normotensive and hypertensive pregnant patients when there was no complicating pre-eclampsia. This is in accord with findings in the non-pregnant subject (Wade et al, 1962). To account for the hypertension there must be increased peripheral resistance in a site or sites other than skin and skeletal muscle vessels. In the absence of conclusive evidence of decreased regional blood flow elsewhere in hypertensive pregnancy it must be concluded that the major site of

increased peripheral resistance is in the vessels supplying the developing foetus (see page 250).

The blood volume in normotensive and hypertensive pregnancy is not different and not related to pregnanediol excretion. Therefore, if the uterine flow rate is decreased and the cardiac output and the blood volume remain the same there must be an increased flow through an area of lowered peripheral resistance, in this case the skeletal muscle vessels.

If, as Hamilton found, there is increased cardiac output in pre-eclampsia and "labile hypertension" when other workers have shown further decrease in uterine flow rates, then skeletal muscle vessel flow would be expected to increase still further. This study shows that this is, in fact, what happens.

However, this must mean that the effect of progesterone on skeletal muscle vessels is enhanced in some way in hypertensive and pre-eclamptic pregnancy and it may be due to some other factor which releases vasoconstrictor tone. In early pregnancy, when the pulse rate and cardiac output are already significantly raised over non-pregnant levels (Walters et al, 1966; and Lees et al, 1967) and progesterone levels are already higher than those found during the menstrual cycle, the fore-arm blood flow rates are significantly lower than the non-pregnant rates and those induced by progestogen administration. Some vaso-constrictor mechanism must be at work at this time, which is specific to pregnancy and independent of oestrogen and progesterone. That it is active in both skeletal and skin vessels is demonstrated by the following evidence.

In early pregnancy, the body temperature is significantly raised above the non-pregnant level for the same subject. Koroxenidis et al (1961) confirmed previous work which showed that raising the body temperature increased cardiac output, digital blood flow rate and fore-arm blood flow rate. The cardiac output and skin flow in digits rose within five minutes of the onset of body heating and the fore-arm blood flow began to rise ten minutes after the onset of heating. Over the temperature rise 97.8 to 98.6°F. (which represented the mean values for non-pregnant and early pregnancy respectively) as found in this study, the cardiac output rose by approximately 1.5 litres per minute and the fore-arm flow by about 4,0 mls./100 mls./minute. McGirr (1952), Edholm et al (1956) and Roddie et al (1956) have shown that this increase in fore-arm flow is exclusively due to the increase in skin flow. Barcroft et al (1955) agreed with this and also noted that in some patients the muscle flow actually decreased. Fox et al (1961) showed that after 12 daily episodes of raising body temperature the fore-arm blood flow at normal body temperature had not altered but there was an exaggerated increase in flow rate in response to body heating. It is not known what response is obtained from prolonged body heating. If it is assumed that these effects are not transitory, remembering that subjects are rarely examined before 8 weeks after the last menstrual period, or 6 weeks after conception, this rise in body temperature may account for the rise in cardiac output early in pregnancy. To substantiate this theory, on examining the mean cardiac output in pregnancy described by Walters et al (1966) in conjunction with the mean body temperature in pregnancy obtained in the present series, it appeared that the two parameters changed

in parallel during pregnancy. Walters study was carried out using the same experimental design as that in the present study. Furthermore, the patients, though different, were examined in the same room in the same hospital and therefore, under the same controlled prevailing conditions, and were selected from the same population. Calculation of a regression line of the mean cardiac output on the mean body temperature gave b = 1.385 $\pm$ S.D. 0.06, giving t = 3.675 on 7 degrees of freedom, $0.01 > P > 0.001$. This is a high degree of correlation, especially considering that the patients were different. (Unfortunately, Walters did not enumerate the body temperatures of his patients, either in his Ph.D. Thesis (1964) or his paper in 1966, so that the correlation cannot be tested within subjects.) It would appear therefore that body temperature plays an important part in cardiac output in pregnancy. This being so, there must be some active vaso-constrictor mechanism at work on the peripheral circulation in early pregnancy sufficient to abolish the rise of hand flow rate associated with increased body temperature and revealing or potentiating a decrease in the fore-arm flow rates. No change in hand flow rate, compared with the non-pregnant level, was found until 20 weeks gestation and the fore-arm flow rate was actively decreased in all blood pressure groups at least until 16 weeks gestation. This shows that a vaso-constrictor mechanism in early pregnancy must act on skin vessels and probably also on skeletal muscle vessels. It is a mechanism which, in some way, is antagonised earlier in hypertensive pregnancy than normotensive pregnancy.

Assali et al (1952) gave 400 mg. tetra-ethyl ammonium chloride intravenously to non-pregnant and pregnant women, to block autonomic

ganglia. Very little effect in reducing the blood pressure was produced in the non-pregnant subject, but an increasing effect was found in normotensive pregnancy until three days after delivery when the effect had disappeared. They noted that no effect was produced in pre-eclamptic pregnancy and that the hypotensive effect of the drug disappeared some weeks before pre-eclampsia was diagnosed. They concluded from this experiment that vessel tone was much more dependent on sympathetic control during pregnancy than in the non-pregnant state but suggested that vessel tone in pre-eclampsia was maintained by a humoral agent. In fact, their findings are in accordance with those found in this study, namely,that there is an increased peripheral vasoconstrictor effect in normotensive pregnancy, hence the exaggerated response to autonomic blockage, and that there is a release of vasoconstrictor tone in pregnancy complicated by hypertension, hence the failure to evoke a response. It is also significant that they found the effect of autonomic blockade to wear off several weeks before clinical pre-eclampsia occurred, which is in accord with the finding that fore-arm blood flow rates increase before there is an increase in blood pressure.

This vasoconstrictor effect and its release is probably not a simple expression of balance between oestrogen and progesterone alone because largest increases in blood flow rates were found when there was little change in balance between these two hormones as reflected in the cornification index. However, more detailed study would have to be carried out to elucidate this point, and, in particular, enquiry made into interactions of various hormones which change during pregnancy. It is interesting to note that the time when the

vaso-constrictor effect is most marked is when chorionic gonadotrophin excretion is at its highest. According to Kitchen (1957) the effect of vasopressin, administered to the non-pregnant subject by intravenous infusion, is to produce an increased fore-arm flow rate, after a transient fall, and a decreased hand flow rate for the duration of the infusion. This effect was reproducible after sympathetic nerve block. The results in hand flow rates are at variance with those found in pregnancy so that it is unlikely that vasopressin has an effect during pregnancy, at least until term approaches, when hand flow rates no longer increase. Kitchen (1959) also studied the effect of infusion of oxytocin on hand and fore-arm blood flow rates. A very transient rise in both was produced and the effect decreased with repetition of the experiment. These investigations were carried out on the non-pregnant subject. It is not known whether similar effects are found in pregnancy, and, in particular, whether there is any synergistic or antagonistic effect produced in the presence of other pregnancy changes. Ahlquist (1947) noted that pitocin produced vasodilatation in uterine muscle in pregnancy and vaso-constriction in the post-partum period. The latter effect was confirmed by Assali et al (1959) who showed that large doses of oxytocics produced an initial increase followed by a marked fall in uterine artery blood flow immediately post-partum. They also showed that a sympatholytic agent (Apresoline) increased the flow substantially.

In the past, the circulatory changes in pregnancy have been likened to those occurring in the presence of an arterio -venous

fistula although this suggestion has been refuted more recently (see page 241). Blood flow rates have been shown to be reduced distal to such a fistula on unilateral experiments in dogs by Henrie et al (1959). The only decrease which takes place in the peripheral circulation, compared with the non-pregnant, occurs early in pregnancy and in the fore-arm, which is not anatomically distal to either uterus or kidney. Abramson et al (1943), Herbert et al (1954 and 1958), Goodrich et al (1964) and Ginsburg et al (1967) showed that either no change at all occurred in the leg blood flow rate or that there was an increase during pregnancy. Thus, peripheral circulatory findings refute the arterio-venous fistula theory.

It has been suggested that the increase in hand flow rate in pregnancy might be due to the increased need for heat loss owing to the metabolism of the developing foetus. There is an increase in basal metabolic rate in some women during pregnancy but not all, as shown by Sandiford et al (1924), Plass et al (1929), Davis (1943) Sontag et al (1944a and b) and Palmer et al (1949). However, hand flow rates increased in all patients during pregnancy. The time at which the basal metabolic rate begins to rise and is maximal have not been elucidated. Palmer et al found increased basal metabolism early in pregnancy and state that they were unable to determine any trend during pregnancy, whereas, a steady increase in hand flow rate occurred during pregnancy from 16 weeks gestation. Hand flow rates have been studied in the non-pregnant hyperthyroid state by Abramson et al (1942) who showed that there was a decrease in flow rate following thyroidectomy in some but not all patients. Both Abramson et al and Eichna et al (1941) showed a decrease in fore-arm blood flow rate after successful thryroidectomy. Sandiford et al and Sontage et al

stress the relationship between birth weight and gain in metabolic rate. The latter also state that women with the lowest non-pregnant basal metabolic rate tended to havethe highest gains in pregnancy. Davis is emphatic that there is no increase in basal metabolism during pregnancy if adequate iodine is given. It is apparent that further work needs to be carried out to clarify this subject in pregnancy. If it is taken as true that the larger the baby the larger the increase in basal metabolic rate and, therefore, the larger the need for heat loss, one would expect a correlation between increase in hand flow rates in pregnancy and birth weight. In this study no relationship could be established between birth weight and either hand or fore-arm increase in flow rate, and there was no relationship between peripheral flow rates and weight gain during pregnancy.

In conclusion, this study has shown that in early pregnancy fore-arm blood flow rates are decreased and that as pregnancy advances an increase occurs which is proportional to the degree of increase of diastolic pressure and inversely proportional to the degree of increase of pregnanediol excretion and change in cornification index. Hand flow rates increase with advancing pregnancy but the numbers examined were too small to establish a correlation with blood pressure.

It has been postulated that there is an active vaso-constrictor mechanism present in early pregnancy which acts both on skin and skeletal muscle vessels and which is antagonised in skeletal muscle vessels earlier in pregnancy complicated by hypertension than in normotensive pregnancy. Evidence has been brought to substantiate

this view. It has also been shown that the effect is not solely due to an interaction of progesterone and oestrogen alone. Further, it has been stressed that changes in fore-arm flow rates precede the changes in blood pressure and are not the result of hypertension None of the indirect evidence supported the view that hand flow rate change was proportional to the heat loss requirement in pregnancy.

# REFERENCES

## REFERENCES

1. Abramson, D. I. and Ferris, E. B. (1940)

Responses of blood vessels in the resting hand and forearm to various stimuli.
Amer.Heart J., 19, 541.

2. Abramson, D. I. and Fierst, S. M. (1942)

Resting blood flow and peripheral vascular responses in hypertensive subjects.
Amer.Heart J., 23, 84.

3. Abramson, D. I. and Fierst, S. M. (1942)

Resting peripheral blood flow in the hyperthyroid state.
Arch.intern.Med., 69, 409.

4. Abramson, D. I., Fierst, S. M. and Flachs, K. (1943)

Resting peripheral blood flow rates in the anaemic state.
Amer.Heart.J., 25, 609.

5. Abramson, D. I., Flachs, K. and Fierst, S. M. (1943)

Peripheral blood flow during gestation.
Amer.J.Obstet.Gynec., 45, 666.

6. Abramson, D. I., Zazeela, H. and Marrs, J. (1939a)

Plethysmographic studies of peripheral blood flow in man.
1. Criteria for obtaining accurate plethysmographic data.
Amer.Heart.J., 17, 194.

7. Abramson, D. I., Zazeela, H. and Marrs, J. (1939b)

2. Physiologic factors affecting resting blood flow in the extremities.
Amer.Heart J., 17, 206.

8. Adams, J. Q. (1954)

Cardiovascular physiology in pregnancy: studies with the dye dilution technique.
Amer.J.Obstet.Gynec., 67, 741.

9. Ahlquist, R. P. and Woodbury, R. A. (1947)

Influence of drugs and uterine activity upon blood flow.
Fed.Proc., 6, 305.

10. Allen, W. I., Barcroft, H. and Edholm, O. G. (1946)

On the action of adrenaline on the blood vessels in human skeletal muscle.
J. Physiol.(Lond.), 105, 255.

11. Allwood, M. J. (1956)

The "after drop" in venous occlusion plethysmography.
Circulat.Res., 4, 268.

12. Allwood, M. J. (1958)

Blood Flow in the foot and calf in the elderly. A comparison with that in young adults.
Clin.Sci., 17, 331.

13. Allwood, M. J., Barcroft, H., Hayes, J. P. L. A. and Hirsjärvi, E. A. (1959)

The effect of mental arithmetic on the blood flow through normal, sympathectomized and hyperhidrotic hands.
J.Physiol.(Lond.), 148, 108.

14. Andros, G. J. (1945)

Blood pressure in normal pregnancy.
Amer.J.Obstet.Gynec., 50, 300.

15. Assali, N. S., Vergon, J. M., Tada, Y. and Garber, S. T. (1952)

Studies on autonomic blockade.VI. The mechanisms regulating the haemodynamic changes in the pregnant woman and their relation to the hypertension of toxaemia of pregnancy.
Amer.J.Obstet.Gynec., 63, 978.

16. Assali, N. S., Dasgupta, K. and Kolin, A. (1959)

Measurement of uterine blood flow and metabolism. VI. Effects of oxytocin, vasopressor and vaso-depressor drugs on the blood flow in the post-partum uterus of unanaesthetised sheep.
Amer.J.Obstet.Gynec., 78, 313.

17. Assali, N. S., Douglas, R. A., Baird W. W., Nicholson, D. B. and Suyemoto, R. (1953)

Measurements of uterine blood flow and uterine metabolism. IV. Results in normal pregnancy.
Amer.J.Obstet.Gynec., 66, 248.

18. Assali, N. S., Rauromo, L and Peltonen, T. (1960)

Measurement of uterine blood flow and uterine metabolism. VIII. Uterine and foetal blood flow and oxygen consumption in early pregnancy.
Amer.J.Obstet.Gynec., 79, 86.

19. Bader, R. A., Bader, M. E., Rose, D. J. and Braunwald, E. (1955)

J.clin.Invest., 34, 1524.

20. Barcroft, H., Bock, K. D., Hensel, H. and Kitchin, A. H. (1955)

Die Muskeldurchblutung des Mensehen bei Indirecter Erwärmung and Abkühlung.
Pflüg.Arch.ges.Physiol., 261, 199.

21. Barcroft H., Brod, J., Hejl, Z., Hirsjärvi, E. A. and Kitchin, A. H. (1960)

The mechanism of the vasodilatation in the fore-arm muscle during stress (mental arithmetic).
Clin.Sci., 19, 577.

22. Barcroft, H. and Edholm, O. G. (1943)

The effect of temperature on blood flow and deep temperature in the human fore-arm.
J.Physiol. (Lond.), 102, 5.

23. Barcroft, H. and Edholm, O. G. (1945)

On the vasodilatation in human skeletal muscle during post-haemorrhagic fainting.
J.Physiol.(Lond.), 104, 161.

24. Barcroft, H. and Swan, H. J. C. (1953)

Sympathetic control of human blood vessels.
Monograph of the Physiological Society, No. 1.
Edward Arnold and Co., London.

25. Bean, W. B. (1945)

The cutaneous arterial spider; a survey.
Medicine (Baltimore), 24, 243.

26. Bean, W. B., Dexter, M. W. and Cogswell, R. C. (1947)

Vascular spiders and palmar erythema in pregnancy.
J.clin.Invest., 26, 1173.

27. Bean, W. B., Cogswell, R., Dexter, M. and Embick, J. F. (1949)

Vascular changes in the skin in pregnancy.
Surg.Gynec.Obstet., 88, 739.

28. Blair, D. A., Golenhofen, K. and Seidel, W. (1959)

Muscle flow during emotional stress.
J.Physiol.(Lond.), 149, 61P.

29. Booth, R. T., Stern, M. I., Wood, C., Sharples, J. J. H. and Pinkerton, J. H. M. (1965)

Urinary hormone excretion in abnormal pregnancy. J.Obstet.Gynaec.Brit.Cwlth., 72, 229.

30. Bӧrell, U., Fernström, I. and Westman, A. (1953)

Hormonal influences on the uterine arteries. An arteriographic study in the human. Acta obstet.gynec.scand., 32, 271.

31. Brehm, H. and Kindling, E. (1955)

Der Kreislauf wӓhrend Schwangerschaft and Wochenbett. (The circulation in pregnancy and the puerperium) Arch.Gynӓk., 185, 696)

32. Brigden, W., Howarth, S. and Sharpey-Shafer, E. P. (1950)

Postural changes in peripheral blood flow of normal subjects with observations on vasovagal fainting reactions as a result of tilting, lordotic position, pregnancy and spinal anaesthesia. Clin.Sci., 9, 79.

33. Brosens, I. (1964)

A study of the spiral arteries of the decidua basalis in normotensive and hypertensive pregnancies. J. Obstet.Gynaec.Brit.Cwlth., 71, 222.

34. Brown, E., Sampson, J. J., Wheeler, E. O., Gundelfinger, B.F. and Giansiracusa, J. E. (1947)

Physiologic changes in the circulation during and after obstetric labor. Amer.Heart.J., 34, 311.

35. Browne, J. C. McC. and Veall, N. (1953)

The maternal placental blood flow in normotensive and hypertensive women. J.Obstet.Gynaec.Brit.Emp., 60, 141.

36. Bucht, H. (1951)

Studies on renal function in man with special reference to glomenular filtration and renal plasma flow in pregnancy. Scand.J.clin.Lab.Invest.,Suppl.3.

37. Burt, C. C. (1949)

Peripheral skin temperature in normal pregnancy. Lancet, 2, 787.

38. Burt, C. C. (1950)

The peripheral circulation in pregnancy.
Trans.Edin.Obstet.Soc. in Edin.med.J., 57, 18.

39. Burton, A. C. (1954)

A critical survey of methods available for the measurement of human peripheral flow.
in "Peripheral Circulation in Man", Ciba Foundation Symposium; Churchill Ltd., London.

40. Burwell, C. S. (1938)

The placenta as a modified arterio-venous fistula, considered in relation to the circulatory adjustments in pregnancy.
Amer.J.med.Sci., 195, 1.

41. Burwell, C. S. (1938)

A comparison of the pressures in arm veins and femoral veins with special references to changes during pregnancy.
Ann.intern.Med., 11. 1305.

42. Burwell, C. S., Strayhorn, W. D., Flickinger, D., Corlette, M.B. Bowerman, E. P. and Kennedy, J. A.

Circulation during pregnancy.
Arch.intern.Med., 62, 979.

43. Buxton, C. L. and Atkinson, W. B. (1948)

Hormonal factos involved in the regulation of basal body temperature during the menstrual cycle and pregnancy.
J.clin.Endocr., 8, 544.

44. Carey, H. M., (1963)

Progesterone.
Chapter 7, p. 92, in Modern Trends in Human Reproductive Physiology, I. Butterworths, London.

45. Caton, W. L., Roby, C. C., Reid, D. E., Caswell, R. Maletskos, E. J., Fluharty, R. G. and Gibson, J. G. (1951)

The circulating red cell volume and body haematocrit in normal pregnancy and the puerperium.
Amer.J.Obstet.Gynec., 61, 1207.

46. Chaplin, H.jr. and Mollison, P. L. (1952)

Correction for plasma trapped in the red cell column of the haematocrit.
Blood, 7, 1227.

47. Chessley, L. C., Connell, E. J., Chessley, E. R., Katz, J. D. and Glissen, C. S. (1946)

The diodrast clearance and renal blood flow in toxaemias of pregnancy.
J.clin.Invest., 19, 219.

48. Chessley, L. C. and Sloan, D. M. (1964)

The effect of posture on renal function in late pregnancy.
Amer.J.Obstet.Gynec., 89, 754.

49. Ciba Foundation Symposium (1954)

Peripheral Circulation in Man.
J. & A. Churchill Ltd., London.

50. Clausen, D. F. and Lifsen, N. (1956)

Determination of Evans Blue Dye in Blood and Tissues.
Proc.Soc.exp.Biol. & Med., 91, 11.

51. Cohen, H. E. and Thomson, K. J. (1936)

Studies on the circulation in pregnancy.
I. The velocity of blood flow and related aspects of the circulation in normal pregnant women.
J.clin.Invest., 15, 607.

52. Cohen, H. E. and Thomson, K. J. (1939)

Studies on the circulation in pregnancy.
X. Summary of studies of the physiology of the circulation of normal pregnant women.
J.Amer.med.Ass., 112, 1556.

53. Cooper, K. E., Edholm, O. G. and Mottram, R. R. (1955)

The blood flow in skin and muscle of the human fore-arm.
J.Physiol.(Lond.), 128, 258.

54. Cope, I. (1958)

Plasma and blood volume changes in late and prolonged pregnancy.
J.Obstet.Gynaec.Brit.Emp., 65, 877.

55. Cope, I. (1961)

Plasma and blood volume changes in pregnancies complicated by pre-eclampsia.
J.Obstet.Gynec.Brit.Cwlth., 68, 413.

56. Courtice, F. C. (1943)

The blood volume of normal animals.
J. Physiol.(Lond.), 102, 290.

57. Crawford, H. G. and Leeper, R. W. (1950)

Diseases of the skin in pregnancy.
Arch.Derm.Syph., Chicago, 61, 753.

58. Crooke, A. C. and Morris, C. J. O. (1942)

The determination of plasma volume by the Evans Blue Method.
J.Physiol. (Lond.), 101, 217.

59. Dahlstrom, H. and Ihrman, K. (1960)

A clinical and physiological study of pregnancy in material from northern Sweden.
1. Observations with special regard to the cardio-pulmonary function during the first trimester of pregnancy.
Acta.Soc.Med(Uppsala), 65, 117.

60. Dahn, I. (1964)

On the calibration and accuracy of segmental calf plethysmography with a description of a new expansion chamber and a new sleeve.
Scand.J.clin.Lab.Invest., 16, 347.

61. Dahn, I. (1965)

Clinical use of the venous occlusion plethysmograph.
Acta.chir.scand., 130, 42.

62. Davidson, S. (1966)

The Principles and Practice of Medicine, 8th edition.
E & S Livingstone Ltd., Edinburgh.

63. Davis, C. H. (1943)

Hypothyroidism as a problem in women.
Amer.J.Obstet.Gynec., 46, 85.

64. Davis, M. E. (1946)

The clinical use of oral basal temperatures.
J.Amer.med.Ass., 130, 929.

65. Dieckmann, W. J. and Wegner, C. R. (1934a)

Blood in normal pregnancy. 1. Blood and plasma volumes.
Arch.intern.Med., 53, 71.

66. Dieckmann, W. J. and Wegner, C. R. (1934b)

Blood in normal pregnancy. 2. The haemoglobin, packed cell volume and erythrocyte determinations and the total amount of variation of each.
Arch.intern.Med., 53, 198.

67. Dixon, H. G. and Robertson, W. B. (1958)

A study of the vessels of the placental bed in normotensive and hypertensive women.
J.Obstet.Gynec.Brit.Emp., 65, 803.

68. Dixon, H. G., Browne, J. C. M. and Davey, D. A., (1963)

Choriodecidual and myometrial blood flow.
Lancet, I, 369.

69. Dúbois and Dubois. (1916)

Arch.intern.Med., 17, 863.
quoted in Documenta Geigy Scientific Tables, 6th edition.
Geigy Pharmaceutical Co. Ltd., Manchester.

70. Duncan, S. L. B. and Ginsburg, J. (1968)

Peripheral circulation in multiple pregnancy.
Amer.J.Obstet.Gynec., 101, 223.

71. Duncan, S. L. B. and Ginsburg, J., (1968)

Arteriolar distensibility in hypertensive pregnancy.
Amer.J.Obstet.Gynec., 100, 222.

72. Duff, R. S. (1956)

Circulation in the hands in hypertension.
Brit.med.J., 2, 974.

73. Eder, H. A. (1959)

The effects of sex hormones on serum lipids and lipo-proteins.
Chapter 24, page 335, in Hormones and Atherosclerosis,
Edited by Pincus, G. Academic Press Inc. New York.

74. Edholm, O. G., Fox, R. H. and Macpherson, R. K. (1956)

The effect of body heating on the circulation in skin and muscle.
J.Physiol.(Lond.), 134, 612.

75. Eichna, L. W. and Wilkins, R. W. (1941)

Blood flow in the fore-arm and calf.
IV. Thyroid activity; observations on the relation of blood flow to basal metabolic rate.
Bull.Johns Hopk.Hosp., 68, 512.

76. Eisenberg, S., Wolf, P. C. (1965)

Plasma volume after posture change in hypertensive subjects.
Arch.intern.Med., 15, 17.

77. Fencl., V., Hejl, Z., Jirka, J., Madlafousek, J. and Brod, J. (1959)

Changes of blood flow in fore-arm muscle and skin during an acute emotional stress (mental arithmetic).
Clin.Sci., 18, 491.

78. Fernström , I (1955)

Arteriography of the uterine artery. Its value in the diagnosis of uterine fibromyoma, tubal pregnancy, adrenal tumour and placental site localisation in cases of intra-uterine pregnancy.
Acta.Radiol.Suppl., 122, 1-128.

79. Ferrebee, J. W., Leigh, O. C. and Berliner, R. W. (1941)

Passage of the Blue Dye T-1824 from the blood stream into the lymph.
Proc.Soc.exp.Biol.Med., 46, 549.

80. Ferris, E. B. and Abramson, D. I. (1940)

Description of a new plethysmograph.
Amer.Heart J., 19, 233.

81. Figar, S. (1959)

Some basic deficiencies of the plethysmographic method and possibilities of avoiding them.
Angiology., 10, 120.

82. Fisher, R. A. and Yates, R.

Statistical tables for biological, agricultural and medical research.
Oliver and Boyd, 98 Great Russell Street, London, 6th edition.

83. Fouts, J. R., Kamm, J. J. and Brodie, B. B. (1957)

Enzymatic reduction of prontosil and other azo dyes.
J. Pharmacol., 120, 291.

84. Fox, R. H., Goldsmith, R., Kidd, D. J. and Lewis, H. E. (1961)

Changes in peripheral blood flow with heat acclimatization.
J.Physiol.(Lond.), 157, 57P.

85. Freeman, N. E. (1935)

The effect of temperature on the rate of blood flow in the normal and in the sympathectonized hand.
Amer.J.Physiol., 113, 384.

86. Gemzell, C. A., Robbe, H. and Sjöstrand, T. (1954)

Blood volume and total amount of haemoglobin in normal pregnancy and the puerperium.
Acta.obstet.gynec.scand., 23, 289.

87. Gibson, J. G. and Evans, W. A. (1937a)

Clinical studies of the blood volume.
I. Clinical application of a method employing the azo dye Evans Blue and the spectrophotometer.
J.clin.Invest., 16, 301.

88. Gibson, J. G. and Evans, W. A. (1937b)

Clinical studies of the blood volume.
II. The relation of plasma and total blood volume to venous pressure, blood velocity rate, physical measurements, age and sex in 90 normal humans.
J.clin.Invest., 16, 317.

89. Gibson, J. G. and Gregerson, M. I. (1935)

Toxicity of two vital dyes used in plasma volume estimations.
Amer.J.Physiol., 113, 50.

90. Gibson, J. G., Peacock, W. C., Seligman, A. M. and Sack, T.(1946)

Circulating red cell volume measured simultaneously by the radio-active iron and dye methods.
J.clin.Invest., 25, 838.

91. Ginsburg, J. and Duncan, S. L. B. (1967)

Peripheral blood flow in normal pregnancy.
Cardiovasc.Res., 1, 132.

92. Ginsburg, J. and Duncan, S. L. B. (1967)

Peripheral circulation in hypertensive pregnancy.
Cardiovasc.Res., 1, 356.

93. Goldring, W., Chasis, H., Ranges, H. A. and Smith, H.W. (1941)

Effective renal blood flow in subjects with essential hypertension.
J.clin.Invest., 20, 637.

94. Goodrich, S. M. and Wood, J. E. (1964)

Peripheral venous distensibility and velocity of venous blood flow during pregnancy or during oral contraceptive therapy.
Amer.J.Obstet.Gynec., 90, 740.

95. Grant, R. T. and Pearson, R. S. B. (1938)

The blood circulation in the human limb; observations on the differences between the proximal and distal parts and remarks on the regulation of body temperature.
Clin.Sci., 3, 119.

96. Green, H. D., Lewis, R. N., Nickerson, N. D. and Heller, A. L. (1944)

Blood flow, peripheral resistance and vascular tonus, with observations on the relationship between blood flow and cutaneous temperature.
Amer.J.Physiol., 141, 518.

97. Greenfield, A. D. M. (1954)

A simple water-filled plethysmograph for the hand or fore-arm, with temperature control.
J. Physiol.(Lond.), 123, 62.

98. Greenfield, A. D. M., Shepherd, J. T. and Whelan, R. F. (1951)

The proportion of the total hand blood flow passing through the digits.
J.Physiol.(Lond.), 113, 63.

99. Greenstein, N. M. and Clahr, J. (1937)

Circulation time studies in pregnant women.
Amer.J.Obstet.Gynec., 33, 414.

100. Gregerson, M. I., Gibson, J. J. and Stead, E. A. (1935)

Plasma volume determination with dyes: errors in colorimetry: use of the blue dye T-1824.
Amer.J.Physiol., 113, 54.

101. Gregerson, M. I. and Schiro, H. (1938)

The behaviour of the dye T-1824 with respect to its absorption by red blood cells and its fate in blood undergoing coagulation.
Amer.J.Physiol., 121, 284.

102. Greig, M., Coyle, M. G., Cooper, W. and Walker, W. (1962)

Plasma progesterone in mother and foetus in the second half of human pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 69, 772.

103. Hamilton, H. F. H. (1949)

Cardiac output in normal pregnancy as determined by the Cournand right heart catheterisation technique.
J.Obstet.Gynaec.Brit.Emp., 56, 548.

104. Hamilton, H. F. H. (1950)

Cardiac output in pregnancy.
Trans.Edin.Obstet.Soc. in Edin.Med.J., 57:1.

105. Hamilton, W. F. and Dow, P. (1963)

Handbook of Physiology, Section 2, Circulation, Vol.II.
American Physiology Society, Washington.

106. Harvey, William (1628 and 1635)

The circulation of the blood and other writings.
Translated by Franklin, K. J. from De Motu Cordis and De Circulatione Sanguinis.
Dent, London, 1966.

107. Hellon, R. F. and Clarke, R. S. J. (1959)

Changes in fore-arm blood flow with age.
Clin.Sci., 18, 1.

108. Henrie, J. N., Johnson, E. W., Wakim, K. G. and Orvis, A. L. (1959)

The influence of experimental arteriovenous fistula on the healing of fractures and on the blood flow distal to the fistula.
Surg. Gynec. Obstet., 108, 591.

109. Herbert, C. M., Banner, E. A. and Wakim, K. G. (1954)

Circulatory manifestations during pregnancy and non-pregnancy.
Amer.J.Obstet.Gynec., 68, 1553.

110. Herbert, C. M., Banner, E. A. and Wakim, K. G. (1958)

Variations in peripheral circulation during pregnancy.
Amer.J.Obstet.Gynec., 76, 742.

111. Hickam, J. B., Cargill, W. H. and Golden, A. (1948)

Cardiovascular reactions to emotional stimuli; effect on the cardiac output, arteriovenous oxygen difference, arterial pressure and peripheral resistance.
J.clin.Invest., 27, 290.

112. Hills, M. (1968)

A note on the analysis of growth curves.
Biometrics., 24, 192.

113. Huckabee, W. E. (1962)

Uterine blood flow.
Amer.J.Obstet.Gynec., 84, 1623.

114. Hutchison, R. and Hunter, D. (1955)

Clinical Methods, 12th edition.
Cassell and Co. Ltd., London.

115. Hyman, C. Burnap, D. and Figar, S. (1963)

Bilateral difference in fore-arm blood flow as measured with a capacitance plethysmograph.
J. appl.Physiol., 18, 997.

116. Hyman, C. and Winsor, T. (1960)

The application of the segmental plethysmograph to the measurement of blood flow through the limbs of human beings.
Amer.J.Cardiol., 6, 667.

117. Hytten, F. E., Paintin, D. B., Stewart, A. M. and Palmer, J. H. (1963)

The relation of maternal heart size, blood volume and stature to the birth weight of the baby.
J.Obstet.Gynaec.Brit.Cwlth., 70, 817.

118. Hytten, F. E. and Paintin, D. B. (1963)

Increase in plasma volume during normal pregnancy.
J. Obstet.Gynaec.Brit.Cwlth., 70, 402.

119. Johnson, T. and Clayton, C. G. (1957)

Diffusion of radio-active sodium in normotensive and pre-eclamptic pregnancies.
Brit.med.J., 1, 312.

120. Kaiser, R. (1955)

Oestrogene und Progesteronstaffwechsel.
(Oestrogen and progesterone metabolism)
Klin.Wschr., 33, 15.

121. Kappas, A. Palmer, R. H. and Glickman, P. B. (1961)

Steroid fever.
Amer.J.Med., 31, 167.

122. Katz, L. N. and Pick, R. (1963)

The role of endocrines, stress and heredity on atherosclerosis.
Chapter 35, p.1197 in Handbook of Physiology, Section II, Circulation, Vol. II. Edited by Hamilton, W. F. and Dow, P. American Physiology Society, Washington.

123. Kerr, M. G. (1965)

The mechanical effect of the gravid uterus in late pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 72, 513.

124. Kerr, M. G. (1968)

Cardiovascular dynamics in pregnancy and labour.
Brit,med.Bull., 24, 19.

125. Kerr, M. G., Scott, D. B. and Samuel, E. (1964)

Studies of the inferior vena cava in late pregnancy.
Brit.med.J., 1, 532.

126. Kerslake, D. McK. (1949)

The effect of the application of an arterial occlusion cuff to the wrist on the blood flow in the human fore-arm.
J. Physiol. (Lond.), 108, 451.

127. Kitchin, A. H. (1957)

The effect of pitressin on hand and fore-arm blood flow.
Clin.Sci., 16, 639.

128. Kitchen, A. H., Lloyd, S. M., Pickford, M. (1959)

Some actions of oxytocin on the cardiovascular system in man.
Clin.Sci., 18, 399.

129. Kjellberg, S. R., Lönroth, H., Rudhe, U. and Sjöstrand, T.(1950)

Blood volume and heart volume during pregnancy and the puerperium.
Acta.med.scand., 138, 421.

130. Klopper, A. and Bikiewicz, A. (1963)

Urinary excretion of oestriol and pregnanediol during normal pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 70, 1024.

131. Klopper, A., Michie, E. A. and Brown, J. B. (1955)

A method for the determination of urinary pregnanediol.
J.Endocr., 12, 209.

132. Koroxenidis, G. T., Shepherd, J, T. and Marshall, R. J. (1961)

Cardiovascular response to acute heat stress.
J. appl.Physiol., 16, 869.

133. Kunkel, P and Stead, E. A. (1938)

Blood flow and vasomotor reactions in the foot in health in arteriosclerosis, and in thromboangiitis obliterans.
J.clin.Invest., 17, 715.

134. Landowne, M. and Katz, L. N. (1942)

A critique of the plethysmographic method of measuring blood flow in the extremities of man.
Amer.Heart.J., 23, 644.

135. Lees, M. M., Taylor, S. H., Scott, D. B. and Kerr, M. G. (1967a)

The circulatory effects of recumbent postural change in late pregnancy.
Clin.Sci., 32, 453.

136. Lees, M. M., Taylor, S. H., Scott, D. B. and Kerr, M. G. (1967b)

A study of cardiac output at rest throughout pregnancy.
J. Obstet. Gynaec. Brit.Cwlth., 74, 319.

137. Lewis, T. and Grant, R. T. (1925)

Observations upon reactive hyperaemia in man,
Heart, 12, 73.

138. Lister, U. M. (1962.

Changes in the blood in pregnancy, labour and the puerperium.
J.Obstet.Gynaec.Brit.Cwlth., 69, 761.

139. Logfren, R. C., (1942)

Erythema of the palms associated with pregnancy.
Arch.Derm.Syph., 46, 502.

140. Loria, A., Sanchez-Medal, L., Kauffer, N. and Quintanar, E. (1962)

Relationship between body haematocrit and venous haematocrit
in normal, splenomegalic, and anaemic states.
J.lab.clin.Med., 60, 396.

141. Manchester, B. and Loube, S. D. (1946)

The velocity of the blood flow in normal pregnant women.
Amer.Heart J., 32, 215.

142. Mendlowitz, M., Altchek, A. and Naftchi, N. (1958)

The work and force of digital vaso-constriction in
normotensive and hypertensive pregnant women.
Amer.J.Obstet.Gynec., 76, 473.

143. Metcalfe, J., Romney, S. L., Ramsey, L. H., Reid, D. E.
and Burwell, C. S. (1953)

An approach to the measurement of uterine blood flow
in pregnancy.
J.clin.Invest., 32, 589.

144. Metcalfe, J., Romney, S. L., Ramsey, L. H., Reid, D. E.
and Burwell, C. S. (1955)

Estimation of uterine blood flow in normal human pregnancy
at term.
J.clin.Invest., 34, 1632.

145. Mishell, D. R., Wide, L. and Gemzell, C. A. (1963)

Immunological determination of human chorionic gonadotrophin
in serum.
J.clin.Endocr., 23, 125.

146. Moore, P. T. and Myerscough, P. R. (1957)

Clearance rates of radio-sodium from myometrium.
J.Obstet.Gynaec.Brit.Emp., 64, 207.

147. Morris, N., Osborn, S. B. and Wright, H. P. (1956)

Effective uterine blood flow during exercise in normal and pre-eclamptic pregnancies.
Lancet, 270, 481.

148. Munnell, E. W. and Taylor, H. C. (1947)

Liver blood flow in pregnancy - hepatic vein catheterisation.
J.clin.Invest., 26, 952.

149. McCall, M. L.,(1949)

Cerebral blood flow and metabolism in toxaemias of pregnancy.
Surg.Gynec.Obstet., 89, 715.

150. McCausland, A. M., Hyman, C., Winsor, T. and Trotter, A. D. (1961)

Venous distensibility during pregnancy.
Amer.J.Obstet.Gynec., 81, 472.

151. McGaughey, H. S. (1952)

The cause of the blood and vascular alterations of normal pregnancy and pre-eclampsia - eclampsia.
Amer.J.Obstet.Gynec., 64, 1268.

152. MacGillivray, I. (1961)

Hypertension in pregnancy and its consequences.
J.Obstet.Gynaec.Brit.Cwlth., 68, 557.

153. McGirr, E. M. (1952)

The rate of removal of radio-active sodium following its injection into muscle and skin.
Clin.Sci., 11, 91.

154. MacGregor, W. G., Gale, C. W., Simmons, E. and Knight, G. J. (1966)

The urinary excretion of human chorionic gonadotrophin in normal and abnormal pregnancy.
J.Obstet.Gynaec,Brit.Cwlth., 73, 775.

155. McLennan, C. E. and Thouin, L. G. (1948)

Blood volume in pregnancy. A critical review. Preliminary report of results with a new technique.
Amer.J.Obstet.Gynec., 55, 189.

156. MacRae, D. J., Irani, J. B., Bowler, R. G. and Longhurst, P. L. (1964)

A comparison between vaginal cytology and urinary hormone excretion during pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 71, 586.

157. Ogston, A. (1943)

Personal communication to Courtice, F. C.
J.Physiol.(Lond.), 102, 290.

158. Paintin, D. B. (1962)

The size of the total red cell volume in pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 69, 719.

159. Paintin, D. B. (1963)

The haematocrit ratio in pregnancy.
J.Obstet.Gynaec,Brit.Cwlth., 70, 807.

160. Palmer, A. J. and Walker, A. H. C. (1949)

The maternal circulation in normal pregnancy.
J.Obstet.Gynaec.Brit.Emp., 56, 537.

161. Pincus, G. (1959)

Hormones and Atherosclerosis.
Academic Press Inc., New York.

162. Plass, E. D. and Yoakim, W. A. (1929)

Basal metabolism studies in normal pregnant women with normal and pathological thyroid glands.
Amer.J.Obstet.Gynec., 18, 556.

163. Reynolds, S. R. M. (1940)

Gynecic Physiology and the Gynaecologist.
Amer.J.Surg., 48, 175.

164. Reynolds, S. R. M. (1939)

Peripheral vascular action of oestrogen in the human male.
J.clin.Invest., 18, 649.

165. Reynolds, S. R. M. (1963)

Maternal blood flow in the uterus and placenta.
Chapter 45 in Handbook of Physiology, section 2, Circulation, Vol. II, edited by Hamilton, W. F. and Dow, P.
American Physiology Society, Washington.

166. Roddie, I. C. and Shepherd, J. T. (1956)

Reflex nervous control of human skeletal muscle blood vessels.
Clin.Sci., 15, 433.

167. Roddie, I. C., Shepherd, J. T. and Whelan, R. F. (1956)

Evidence from venous oxygen saturation measurements that the increase in fore-arm blood flow during body heating is confined to the skin.
J.Physiol.(Lond.), 134, 144.

168. Romney, S. L., Reid, D. E., Metcalfe, J and Burwell, C.S. (1955)

Oxygen utilization by the human foetus in utero.
Amer.J.Obstet.Gynec., 70, 791.

169. Roscoe, H. H. and Donaldson, G. M. M. (1946)

The blood in pregnancy. Part I; The haemoglobin level.
J.Obstet.Gynaec.Brit.Emp., 53, 430.

170. Roscoe, H. H. and Donaldson, G. M. M. (1946)

The blood in pregnancy. Part II; The blood volume, cell volume and haemoglobin mass in pregnancy.
J.Obstet.Gynaec.Brit.Emp., 53, 527.

171. Rose, T. F. (1949)

The haemangiomata of pregnancy.
J.Obstet.Gynaec.Brit.Emp., 56, 364.

172. Rowntree, L. G., and Browne, G. E. (1929)

The volume of the blood and plasma.
Philadelphia. Quoted by Roscoe et al, 1946.

173. Roy, S. B., Malkan, P. K., Virik, R. and Bhatia, M. L. (1966)

Circulatory effects of pregnancy.
Amer.J.Obstet.Gynec., 96, 221.

174. Russell, C. S. (1965)

Pregnanediol and oestriol excretion in unsuccessful pregnancy.
J. Obstet.Gynaec.Brit.Cwlth., 72, 1031.

175. Sandiford, I. and Wheeler, T. (1924)

Basal metabolism before, during and after pregnancy.
J.biol.Chem., 62, 329.

176. Scott, D. B. and Kerr, M. G. (1963)

Inferior vena caval pressure in late pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 70, 1044.

177. Shearman, R. P. (1959)

Some aspects of urinary excretion of pregnanediol in pregnancy.
J.Obstet.Gynaec.Brit.Emp., 66, 1.

178. Shepherd, J. T. (1951)

Effect of cigarette smoking on blood flow through the hand.
Brit.med.J., 2, 1007.

179. Shepherd, J. T. (1963)

Physiology of the circulation in human limbs in health and disease.
Saunders, Philadelphia.

180. Sims, E. A. H. and Krantz, K. E. (1958)

Serial studies of renal function during pregnancy and the puerperium in normal women.
J.clin.Invest., 37, 1764.

181. Sontag, L. W., Reynolds, E. L. and Torbet, V. (1944)

Status of infant at birth as related to basal metabolism of mother in pregnancy.
Amer.J.Obstet.Gynec., 48, 208.

182. Sontag, L. W., Reynolds, E. L. and Torbet, V. (1944)

Relation of basal metabolic gain during pregnancy to non-pregnant basal metabolism.
Amer.J.Obstet.Gynec., 48, 315.

183. Spetz, S. (1964)

Peripheral circulation during normal pregnancy.
Acta.obstet.gynec.scand., 43, 309.

184. Spetz, S. (1965)

Studies on peripheral circulation in normal pregnancy and in pregnancy complicated by toxaemia and diabetes mellitus.
Acta.obstet.gynec.scand., Suppl.I.

185. Spetz, S. (1965)

Peripheral circulation in pregnancy complicated by toxaemia.
Acta.obstet.gynec.scand., 44, 243.

186. Spetz, S. (1965)

Peripheral circulation in pregnancy complicated by diabetes mellitus.
Acta.obstet.gynec.scand., Suppl.I.

187. Thomson, K. J., Hirsheimer, A., Gibson, J. G. and Evans, W. A. (1938)

Studies on the circulation in pregnancy. Blood volume changes in normal pregnant women.
Amer.J.Obstet.Gynec., 36, 48.

188. Tysoe, F. W. and Lowenstein, L. (1950)

Blood volume and haematological studies in pregnancy and the puerperium.
Amer.J.Obstet.Gynec., 60, 1187.

189. Vanderhoof, E. and Clancy, J. (1962)

Peripheral blood flow as an indicator of emotional reaction.
J.appl.Physiol., 17, 67.

190. Verel, D., Bury, J. D. and Hope, A. (1956)

Blood volume changes in pregnancy and the puerperium.
Clin.Sci., 15, 1.

191. Wachtel, E. G. (1964)

Exfoliative cytology in gynaecological practice.
Butterworths, London.

192. Wade, O. L. and Bishop, J. M. (1962)

Cardiac output and regional blood flow.
Blackwell Scientific Publications, Oxford, England.

193. Walters, W. A. W. (1964)

Studies on the circulation during pregnancy.
A thesis presented for the degree of Doctor of Philosophy in the Faculty of Medicine, University of London.

194. Walters, W. A. W., MacGregor, W. G. and Hills, M. (1966)

Cardiac output at rest during pregnancy and the puerperium.
Clin.Sci., 30, 1.

195. Warren, J. V., Nickerson, J. L. and Elkin, D. C. (1951)

The cardiac output in patients with arterio-venous fistulae.
J.clin.Invest., 30, 210.

196. Wörko, L., Lagerhöf, H., Bucht, H. and Holmgren, A. (1950)

Circulatory changes in pregnancy.
Acta.med.scand., Suppl., p.239.

197. Wörko, L. (1954)

Pregnancy and heart disease.
Acta.obstet.gynec.scand., 33, 162.

198. Whitaker's Almanack (1968)

Temperature, Rainfall and Sunshine, General Values, 1964-67, p.1062, 100th edition.
Compiled from Monthly Weather Report published by the Meteorological Office.
J.Whitaker & Sons, Ltd., 1967,
13 Bedford Square, London, W.C.1.

199. White, R. (1950)

Blood volume in pregnancy.
Trans.Edin.Obstet.Soc. in Edin,med.J., 57, 14.

200. Wilkins, R. W., Eichna, L. W. (1941)

Blood flow to the fore-arm and calf. 1. Vasomotor reactions: Role of the sympathetic nervous system.
Bull.Johns.Hopk.Hosp., 68, 425.

201. Winner, W. (1965)

The role of the placenta in the systemic circulation, a reappraisal.
Obstet.Gynec.Surv., 20, 545.

202. Witts, L. J. (1962)

The blood in pregnancy.
J.Obstet.Gynaec.Brit.Cwlth., 69, 714.

203. Wright, A. D., Dixon, H. G., Joplin, G. F. (1968)

Diabetes and latent diabetes in pregnancy.
Brit.med.Bull., 24, 25.

204. Wright, H. P., Osborn, S. B. and Edmonds, D. G. (1950)

Changes in rate of flow of venous blood in leg during pregnancy measured with radio-active sodium.
Surg.Gynec.Obstet., 90, 481.

# APPENDIX

## Fore-Arm Blood Flows

## Non-Pregnant Control Group

| Interval: | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Mean |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Subjects | Weeks | | | | | | | | | | |
| | 1-3 | 4-7 | 8-11 | 12-15 | 16-19 | 20-23 | 24-27 | 28-31 | 32-35 | 36-39 | |
| No. 1 | 3.9 | 5.9 | 9.0 | 4.0 | 4.2 | 9.1 | 5.3 | 7.0 | 2.4 | 2.1 | 5.3 |
| No. 2 | 2.5 | 1.8 | 1.4 | 2.1 | 1.6 | 1.5 | 1.0 | 1.3 | 1.6 | 2.8 | 1.8 |
| No. 3 | 5.4 | 4.2 | 4.6 | 4.7 | 3.8 | 2.4 | 2.8 | 3.9 | 6.8 | 3.6 | 4.2 |
| No. 4 | 2.6 | 3.1 | 2.7 | 3.1 | 2.9 | 1.3 | 6.2 | 3.1 | 2.9 | - | 3.1 |
| No. 5 | 1.2 | 1.6 | 1.2 | 1.6 | 2.6 | 6.3 | 9.0 | 3.5 | 2.9 | 4.5 | 3.4 |
| No. 6 | 2.2 | 3.2 | 6.4 | 2.6 | 5.3 | 3.9 | 4.5 | 4.5 | - | - | 4.1 |
| No. 7 | 4.5 | 2.4 | 3.4 | 3.2 | 4.0 | 6.0 | - | - | - | - | 4.0 |
| No. 8 | 5.2 | 5.6 | 7.5 | 7.0 | 7.5 | 4.1 | 3.2 | 6.7 | 10.5 | 9.1 | 6.6 |
| No. 9 | 4.0 | 3.7 | 4.1 | 3.0 | 1.7 | 2.5 | 4.0 | 2.1 | 2.0 | 3.5 | 3.1 |
| No. 10 | 7.1 | 5.2 | 8.0 | 5.7 | 2.6 | 2.5 | 7.2 | 6.4 | - | - | 5.6 |
| No. 11 | 2.0 | 0.8 | 2.5 | 2.3 | 4.5 | 5.4 | 2.4 | - | - | - | 2.4 |
| No. 12 | 2.8 | 4.3 | 3.3 | 2.4 | 2.3 | 5.0 | 4.3 | 1.9 | - | - | 3.4 |
| No. 13 | 2.1 | 3.6 | 1.6 | 2.1 | 2.6 | 1.6 | 2.8 | - | - | - | 2.3 |
| No. 14 | 5.4 | 5.4 | 3.2 | 3.6 | 3.7 | 3.4 | - | - | - | - | 4.1 |
| No. 15 | 2.6 | 1.9 | 3.2 | 6.0 | 5.7 | - | - | - | - | - | 3.9 |
| No. 16 | 2.4 | 3.1 | 2.4 | 2.3 | - | - | - | - | - | - | 2.6 |
| No. 17 | 4.2 | 5.0 | 6.6 | - | - | - | - | - | - | - | 5.3 |

Cont.

Fore-Arm Blood Flows; Non-Pregnant Control Group, cont.

| Interval: | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Mean |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Subjects | Weeks | | | | | | | | | | |
| | 1-3 | 4-7 | 8-11 | 12-15 | 16-19 | 20-23 | 24-27 | 28-31 | 32-35 | 36-39 | |
| No. 18 | 8.5 | 2.3 | 4.8 | 12.1 | - | - | - | - | - | - | 6.9 |
| No. 19 | 8.6 | 8.8 | - | - | - | - | - | - | - | - | 8.7 |
| No. 20 | 2.2 | 5.5 | - | - | - | - | - | - | - | - | 3.9 |
| No. 21 | 1.5 | 3.3 | - | - | - | - | - | - | - | - | 2.4 |
| No. 22 | 3.6 | - | - | - | - | - | - | - | - | - | 3.6 |
| No. 23 | 1.3 | - | - | - | - | - | - | - | - | - | 1.3 |
| No. 24 | 2.6 | - | - | - | - | - | - | - | - | - | 2.6 |
| No. 25 | 3.1 | - | - | - | - | - | - | - | - | - | 3.1 |
| No. 26 | 4.3 | - | - | - | - | - | - | - | - | - | 4.3 |
| No. 27 | 4.1 | - | - | - | - | - | - | - | - | - | 4.1 |
| No. 28 | 3.9 | - | - | - | - | - | - | - | - | - | 3.9 |
| No. 29 | 2.6 | - | - | - | - | - | - | - | - | - | 2.6 |
| No. 30 | 1.9 | - | - | - | - | - | - | - | - | - | 1.9 |
| No. 31 | 5.7 | - | - | - | - | - | - | - | - | - | 5.7 |
| No. 32 | 6.7 | - | - | - | - | - | - | - | - | - | 6.7 |
| Mean | 3.8 | 3.8 | 4.2 | 4.0 | 3.7 | 3.9 | 4.4 | 4.0 | 4.2 | 4.2 | 4.0 |
| S.D. | 1.97 | 1.86 | 2.36 | 2.52 | 1.62 | 2.23 | 2.24 | 2.07 | 3.28 | 2.50 | 1.68 |
| S.E. | | | | | | | | | | | 0.30 |
| 99% C.I. | | | | | | | | | | | 0.774 |

Fore-Arm Blood Flow

Normotensive

| Subjects | Ante-Natal - Weeks Gestation | | | | | | | | | | Post-Natal | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 8 - 11 | 12 - 15 | 16 - 19 | 20 - 23 | 24 - 27 | 28 - 31 | 32 - 35 | 36 - 39 | 40 over | 40 (corr.) | 3rd day | 6 weeks | 12 weeks | 40 weeks | 40 (corr.) |
| No. 1 | 1.3 | 2.3 | - | 4.7 | 1.8 | 1.0 | 7.0 | - | - | | 3.5 | 2.3 | 6.4 | - | |
| No. 2 | - | 1.4 | 2.6 | 2.7 | 3.5 | 2.5 | 5.9 | 3.5 | 3.2 | | 2.9 | 3.3 | 6.1 | - | |
| No. 3 | 4.8 | 3.5 | 2.1 | 3.0 | 3.5 | 3.9 | 4.2 | 2.2 | 2.4 | | 3.1 | 3.1 | 4.1 | 3.7 | |
| No. 4 | 1.2 | 2.9 | 2.3 | 1.3 | 2.3 | 2.0 | 3.3 | 1.3 | - | | 1.7 | 2.2 | 8.6 | 4.8 | |
| No. 5 | 2.9 | 3.0 | 5.0 | 2.4 | 2.4 | 2.9 | 1.4 | 3.7 | - | | 4.7 | 2.8 | 2.4 | 2.1 | |
| No. 6 | 2.1 | 6.9 | 1.5 | 1.2 | 2.2 | 3.4 | 5.0 | 6.4 | - | | 12.4 | 2.9 | 1.0 | 6.4 | |
| No. 7 | 1.5 | 1.3 | 2.8 | 1.7 | 2.2 | 4.7 | 3.5 | 2.6 | - | | 1.6 | 2.0 | 2.7 | 4.3 | |
| No. 8 | 1.9 | 3.3 | 3.2 | 3.2 | 1.6 | 1.4 | 2.7 | 1.2 | 1.9 | | 2.0 | 2.2 | 2.4 | 4.4 | |
| No. 9 | 3.0 | 2.4 | 1.9 | 3.9 | 1.6 | 5.0 | 1.6 | 1.5 | 6.9 | | 3.1 | 1.6 | 1.8 | - | |
| No. 10 | 4.8 | 3.9 | 5.2 | 1.4 | 2.0 | 1.5 | 2.4 | 4.7 | 4.7 | | 4.6 | 5.8 | 7.0 | 4.4 | |
| No. 11 | 1.5 | 1.7 | 1.4 | 1.4 | 1.4 | 3.7 | 3.3 | 2.2 | - | | - | 4.2 | 8.4 | 4.9 | |
| No. 12 | - | 2.8 | 3.3 | 3.8 | 3.4 | 2.9 | 4.2 | 2.3 | - | | 8.7 | 5.2 | 7.1 | - | |
| No. 13 | 3.5 | 3.7 | 2.9 | 3.0 | 3.1 | 5.8 | 2.4 | 6.8 | - | | 5.0 | 2.4 | 2.4 | - | |
| No. 14 | - | 1.2 | 1.1 | 1.0 | 1.9 | 1.4 | 2.2 | - | - | | 4.4 | 1.4 | 4.2 | 3.2 | |
| No. 15 | 2.0 | 1.4 | 1.6 | 2.1 | 1.6 | 1.7 | 3.7 | 1.9 | 3.5 | | 5.0 | 2.7 | 2.2 | 9.0 | |
| No. 16 | 1.8 | 1.4 | 0.8 | 1.0 | 2.5 | 2.2 | 1.3 | - | - | | 1.8 | 2.1 | 2.1 | - | |
| No. 17 | 1.6 | 1.6 | 1.9 | 3.2 | 4.2 | 3.1 | 1.5 | 1.4 | - | | - | 3.1 | 3.2 | 6.1 | |
| No, 18 | 2.5 | 2.7 | 1.5 | 2.4 | 3.5 | 4.2 | 2.9 | 2.6 | - | | 8.3 | 6.3 | - | - | |
| No. 19 | 2.9 | 5.9 | 1.3 | - | 4.0 | 3.8 | 7.4 | 6.0 | - | | 3.7 | 2.6 | 6.1 | - | |
| No. 20 | - | 3.4 | 2.1 | 1.9 | 4.8 | 3.9 | 1.6 | 1.5 | - | | 3.8 | 2.3 | 5.3 | 2.2 | |
| No. 21 | 2.1 | 1.9 | 1.8 | 3.0 | 3.9 | 4.5 | 6.0 | 1.8 | - | | 3.2 | 3.7 | 5.3 | 1.2 | |
| No. 22 | 2.4 | 3.9 | 2.6 | 2.4 | 3.4 | 2.2 | 1.8 | 3.4 | 2.1 | | 3.1 | 5.4 | 3.8 | 1.9 | |
| No. 23 | 1.5 2.7 | 1.1 | 1.4 | 4.1 | 1.4 | 1.9 | 2.5 | - | - | | 2.8 | 1.5 | 4.0 | 2.3 | |
| No. 24 | 3.0 | 7.4 | 6.1 | 5.7 | 9.4 | 1.0 | 6.6 | 7.1 | 5.2 | | 5.0 | 2.4 | 11.8 | - | |
| No. 25 | 3.0 | 7.9 | 6.7 | 4.0 | 7.6 | 13.9 | 3.5 | - | - | | 5.8 | 3.7 | 3.3 | - | |
| No. 26 | 3.9 5.1 | 4.1 | 4.3 | 4.3 | 7.2 | 4.2 | 2.1 | 3.2 | 4.9 | | 9.2 | 3.3 | - | - | |
| Mean | 2.6 | 3.2 | 2.7 | 2.8 | 3.3 | 3.4 | 3.5 | 3.2. | 3.9 | 3.9 | 4.6 | 3.1 | 4.7 | 4.1 | 4.4 |
| S.D. | 1.05 | 1.89 | 1.59 | 1.26 | 2.02 | 2.51 | 1.83 | 1.91 | 1.68 | | 2.67 | 1.32 | 2.63 | 2.06 | |
| S.E. | 0.22 | 0.37 | 0.32 | 0.25 | 0.40 | 0.49 | 0.36 | 0.42 | 0.56 | | 0.55 | 0.26 | 0.54 | 0.53 | |

Fore-Arm Blood Flow Rates - Hypertension I Group.

| Subjects | Ante-Natal - Weeks Gestation | | | | | | | | | | Post-Natal | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 8 -11 | 12 -15 | 16 -19 | 20 -23 | 24 -27 | 28 -31 | 32 -35 | 36 -39 | 40 over | 40 (corr.) | 3rd day | 6 weeks | 12 weeks | 40 weeks | 40 (corr.) |
| No. 1 | 1.6 | - | 1.5 | 1.2 | 1.7 | 7.3 | 4.6 | 2.4 | - | | 1.2 | 1.4 | 1.6 | 4.2 | |
| No. 2 | 2.0 | 2.3 | 3.8 | 1.9 | 5.0 | 1.4 | 6.1 | 6.8 | - | | 3.1 | 2.6 | 1.9 | 4.2 | |
| No. 3 | - | 1.4 | 2.6 | 2.9 | 3.3 | 2.4 | 1.6 | 3.9 | 2.8 | | 4.2 | 8.1 | 3.0 | 3.5 | |
| No. 4 | 3.3 | 1.8 | 1.9 | 2.1 | 1.9 | 2.5 | 4.1 | 2.5 | - | | 5.2 | 5.0 | 3.0 | 3.9 | |
| No. 5 | - | 6.4 | 2.3 | 3.3 | 2.4 | 1.3 | 2.1 | 8.6 | - | | 7.6 | 2.5 | 2.3 | 5.1 | |
| No. 6 | 5.4 4.2 | 6.8 | 3.4 | 3.1 | 2.6 | 1.9 | 3.6 | 2.9 | - | | 3.7 | 3.0 | 2.6 | 5.2 | |
| No. 7 | 2.2 2.2 | 1.4 | 1.0 | 7.0 | 2.9 | - | 4.4 | 5.2 | - | | 3.7 | 1.9 | 3.1 | - | |
| No. 8 | 2.9 | 2.6 | 5.6 | - | 2.8 | 3.4 | 4.9 | 2.3 | - | | 8.5 | 3.1 | 3.3 | - | |
| No. 9 | 1.9 | - | 1.6 | 1.5 | 1.6 | 1.0 | 1.6 | 1.0 | - | | 5.8 | 1.3 | 1.9 | - | |
| No.10 | 1.7 | 2.3 | 1.8 | 2.1 | 3.9 | - | 1.7 | 2.0 | - | | 3.3 | 1.2 | 1.8 | - | |
| No.11 | 4.0 4.5 | 3.3 | 2.6 | 2.4 | 5.7 | 4.9 | 8.6 | 6.1 | - | | 3.4 | 2.0 | - | - | |
| No.12 | 1.9 | 2.1 | 1.7 | 1.5 | - | 4.6 | 6.7 | 2.5 | 1.6 | | 2.0 | 2.9 | 3.5 | 4.5 | |
| No.13 | 4.0 | 4.0 | 4.9 | 2.0 | 4.1 | 2.9 | 4.5 | 5.6 | - | | 5.3 | 4.4 | 1.1 | 2.6 | |
| No.14 | 3.0 | 2.9 | 2.6 | 8.0 | 7.6 | 6.0 | 1.3 | 7.6 | - | | 7.0 | 3.9 | 4.7 | 5.5 | |
| No.15 | 4.6 | 3.0 | 5.3 5.1 | 8.6 | 3.4 | 3.1 | 2.3 | 9.8 | - | | 4.5 | 5.5 | 4.4 | - | |
| No.16 | 2.9 | 6.5 | 7.0 | 4.2 | 9.2 | 4.2 | 7.3 | 4.2 | - | | 4.9 | 3.3 | 5.4 | - | |
| No.17 | 2.3 | 7.0 | 6.0 | 4.9 | 6.3 | 8.9 | 2.9 | 3.7 | - | | 6.8 | 5.9 | - | - | |
| No.18 | 2.9 | 0.9 | 1.3 | 3.6 | 2.6 | 4.3 | 11.8 | 6.7 | - | | 5.4 | 0.8 | - | - | |
| No.19 | 8.5 | 4.4 | 5.2 | 5.5 | 6.1 | 6.0 | 21.1 | 3.3 | 5.9 | | 8.5 | 5.2 | 2.3 | - | |
| No.20 | 4.8 | 3.8 | 6.1 | 4.3 | 4.3 | 9.9 | 2.2 | 5.0 | 6.0 | | 6.7 | 3.3 | 7.0 | - | |
| No.21 | 2.1 2.0 | 2.2 | 2.1 | 2.7 | 2.4 | 2.3 | 2.3 | 12.0 | - | | 6.0 | 2.4 | 1.6 | 2.0 | |
| No.22 | 1.7 | 2.2 | 3.6 | 2.6 | 2.6 | 2.9 | 3.7 | 6.0 | - | | 1.2 | 3.5 | - | - | |
| No.23 | 4.0 | 1.2 | 5.6 | - | 1.3 | 3.4 | - | 1.5 | - | | 1.4 | 3.3 | - | - | |
| No.24 | - | - | 2.1 | 1.9 | 9.8 | 3.5 | 1.4 | 2.0 | - | | 1.0 | - | - | - | |
| Mean | 3.2 | 3.3 | 3.4 | 3.5 | 4.1 | 4.0 | 4.8 | 4.7 | 4.1 | 5.1 | 4.6 | 3.3 | 3.0 | 4.1 | 4.5 |
| S.D. | 1.63 | 1.92 | 1.83 | 2.11 | 2.38 | 2.37 | 4.41 | 2.82 | 2.22 | | 2.28 | 1.74 | 1.52 | 1.13 | |
| S.E. | 0.36 | 0.42 | 0.37 | 0.45 | 0.50 | 0.51 | 0.92 | 0.58 | 1.11 | | 0.47 | 0.36 | 0.36 | 0.36 | |

Fore-Arm Blood Flow Rates - Hypertension II Group

| Subjects | Ante-Natal - Weeks Gestation | | | | | | | | | | Post-Natal | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 8 -11 | 12 -15 | 16 -19 | 20 -23 | 24 -27 | 28 -31 | 32 -35 | 36 -39 | 40 over | 40 (corr.) | 3rd day | 6 weeks | 12 weeks | 40 weeks | 40 (corr.) |
| No. 1 | 2.3 | 3.5 | - | 1.0 | 2.6 | 4.0 | 4.2 | 8.4 | 2.8 | | 8.4 | 3.3 | 6.0 | 3.7 | |
| No. 2 | 3.1 | 3.6 | 4.6 | - | 5.0 | 4.1 | 3.8 | 2.8 | - | | 7.1 | - | - | - | |
| No. 3 | 2.3 | 2.2 | 2.4 | 6.1 | 4.1 | 4.3 | 2.1 | 2.5 | - | | 5.3 | 4.3 | 5.5 | - | |
| No. 4 | 2.6 | 2.7 | 7.4 | 3.6 | 8.3 | 1.3 | 2.0 | 6.9 | - | | 4.5 | 1.6 | 4.5 | - | |
| No. 5 | 3.1 | 3.1 | 1.8 | 2.6 | 1.6 | 1.3 | 3.6 | 6.8 | 9.4 | | 6.2 | 3.6 | 1.7 | 3.1 | |
| No. 6 | 2.9 | 1.6 | 3.5 | 2.7 | 6.5 | 4.6 | 10.5 | 6.6 | - | | 11.0 | 5.0 | 5.5 | 4.0 | |
| No. 7 | 2.1 | 1.5 | 1.7 | 4.6 | 2.3 | 4.9 | 6.0 | 14.5 | - | | 7.1 | 2.3 | 3.7 | - | |
| No. 8 | 2.2 | 5.1 | 3.2 | 2.9 | 4.5 | 3.4 | 2.7 | 9.8 | - | | 2.1 | 3.7 | 6.3 | - | |
| No. 9 | 5.4 | 2.0 | 9.4 | 6.3 | 7.7 | 6.9 | 3.1 | 1.3 | - | | 2.3 | 4.8 | 4.1 | 3.4 | |
| No. 10 | 2.4 | 3.3 | 2.4 | 2.4 | 4.7 | 2.8 | 4.4 | 2.9 | - | | 2.2 | 1.8 | 9.5 | - | |
| No. 11 | 2.3 | 1.6 | 4.8 | 5.1 | 3.0 | 8.2 | 4.8 | 1.4 | 4.4 | | 5.3 | 5.1 | - | - | |
| No. 12 | 3.9 | 4.1 | 7.3 | 4.3 | 3.5 | 4.2 | 4.6 | 7.1 | 3.8 | | 4.0 | 5.2 | 3.3 | - | |
| No. 13 | 3.5 | 1.1 | 9.5 | 2.4 | 2.5 | 10.8 | - | 6.4 | 5.6 | | 4.3 | 4.2 | - | - | |
| No. 14 | 1.9 | 1.7 | 2.6 | 2.4 | 6.2 | 3.2 | 5.1 | 6.8 | 4.6 | | 7.9 | 4.7 | - | - | |
| No. 15 | 2.5 | 3.3 | 3.3 | 2.1 | 3.0 | 4.2 | 2.6 | - | - | | 3.4 | 8.4 | 5.2 | 2.3 | |
| No. 16 | 2.7 | 3.1 | 2.4 | 4.2 | 3.2 | 1.9 | 3.0 | 9.3 | - | | 3.2 | 3.7 | 1.8 | 3.7 | |
| No. 17 | 2.4 | 2.8 | 1.9 | 1.3 | 1.2 | 2.6 | 2.7 | 1.2 | - | | 3.3 | 1.6 | 1.4 | - | |
| No. 18 | 6.8 4.8 | 4.3 | 3.2 | 5.8 | 5.0 | 3.2 | 6.2 | 3.9 | - | | 6.1 | 5.6 | 12.0 | 6.5 | |
| No. 19 | 5.9 | 3.8 | 5.7 | 4.7 | 11.2 | 6.5 | 3.7 | 1.7 | 4.3 | | 4.6 | 5.2 | 9.6 | - | |
| No. 20 | 2.1 | 1.6 | 2.1 | 4.8 | 2.8 | 1.8 | 3.5 | 10.8 | - | | 7.4 | 3.7 | 3.7 | 2.5 | |
| No. 21 | 3.3 | 3.2 | 1.7 | 1.1 | 3.2 | - | 3.0 | 6.5 | 1.9 | | 3.2 | 3.7 | 3.3 | 4.0 | |
| No. 22 | 3.0 | 6.2 | 5.5 | 8.1 | 8.2 | 5.2 | 6.1 | 5.1 | - | | 5.1 | 3.7 | 5.6 | 7.6 | |
| No. 23 | 2.0 0.9 | 1.5 | 0.8 | 2.2 | 1.5 | 1.2 | 6.0 | 2.4 | 2.7 | | 4.3 | - | 3.4 | 8.6 | |
| No. 24 | 4.7 | 3.7 | 4.2 | 7.0 | 7.0 | 9.0 | 1.0 | 9.7 | 9.2 | | 11.9 | 3.7 | - | - | |

cont. over

Hypertension II cont.

| Subjects | Ante-Natal - Weeks Gestation | | | | | | | | | | Post-Natal | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 8 -11 | 12 -15 | 16 -19 | 20 -23 | 24 -27 | 28 -31 | 32 -35 | 36 -39 | 40 over | 40 (corr.) | 3rd day | 6 weeks | 12 weeks | 40 weeks | 40 (corr.) |
| No. 25 | 7.9 | 3.8 | 6.7 | 2.7 | 6.7 | 4.5 | 4.1 | 4.1 | 5.3 | | 8.5 | 1.6 | 4.1 | - | |
| No. 26 | - | - | 6.3 | 3.4 | 16.4 | 1.6 | 4.7 | 8.3 | - | | 4.0 | 5.3 | 2.7 | - | |
| No. 27 | - | 1.9 | 3.3 | 3.5 | 2.1 | 3.8 | 6.1 | 9.6 | 18.5 | | 5.6 | 4.2 | 2.7 | - | |
| No. 28 | - | 6.5 | 6.6 | 3.6 | - | 3.0 | 5.5 | 4.5 | - | | 4.2 | 5.2 | - | - | |
| No. 29 | - | - | 3.9 | 2.9 | 7.3 | 5.8 | 14.3 | 4.8 | - | | 8.8 | 9.0 | - | - | |
| No. 30 | 5.0 | 7.0 | 8.5 | 3.7 | 7.6 | 4.0 | 6.4 | 4.2 | 10.8 | | 6.4 | 5.4 | 3.3 | 11.9 | |
| No. 31 | 2.8 | 1.3 | 2.0 | 2.4 | 1.8 | 1.4 | 1.3 | 1.1 | 2.6 | | 2.6 | 2.0 | 2.0 | 1.6 | |
| No. 32 | - | - | 5.0 | 4.1 | 1.9 | 4.1 | 4.9 | - | - | | - | - | - | - | |
| No. 33 | 5.6 | 2.2 | 5.0 | 1.3 | 3.3 | 2.3 | 6.5 | 4.9 | - | | 5.3 | 2.2 | 10.2 | - | |
| No. 34 | 2.3 | 3.1 | 2.4 | 3.4 | 1.8 | 0.6 | 1.0 | 2.0 | 7.2 | | 2.2 | 1.2 | 1.2 | - | |
| No. 35 | 1.7 | 2.7 | 1.3 | 2.5 | 2.3 | 2.0 | 1.2 | 2.8 | - | | 2.8 | 1.4 | 1.2 | 1.7 | |
| No. 36 | - | - | - | 1.5 | - | 4.3 | 8.9 | 29.3 | - | | 4.1 | 5.1 | - | - | |
| Mean | 3.3 | 3.1 | 4.2 | 3.5 | 4.7 | 3.9 | 4.6 | 6.2 | 6.2 | 7.2 | 5.3 | 3.98 | 4.6 | 4.6 | 5.0 |
| S.D. | 1.54 | 1.40 | 2.39 | 1.71 | 3.24 | 2.29 | 2.71 | 5.21 | 4.34 | | 2.46 | 1.83 | 2.88 | 2.97 | |
| S.E. | 0.28 | 0.25 | 0.41 | 0.29 | 0.56 | 0.39 | 0.46 | 0.89 | 1.12 | | 0.42 | 0.32 | 0.55 | 0.79 | |

| Subjects | Ante-Natal - Weeks Gestation | | | | | | | | | | Post-Natal | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 8 -11 | 12 -15 | 16 -19 | 20 -23 | 24 -27 | 28 -31 | 32 -35 | 36 -39 | 40 over | 40 (corr.) | 3 days | 6 weeks | 12 weeks | |
| No. 1 | 9.3 | 6.0 | 7.7 | 5.9 | 16.0 | 21.3 | 17.1 | 14.5 | 19.6 | | 8.1 | 11.8 | - | N |
| No. 2 | 8.5 | 6.4 | 17.4 | 19.2 | 18.5 | 19.6 | 12.2 | 24.5 | - | | 11.9 | 4.7 | 6.0 | N |
| No. 3 | 8.1 | 7.0 | 10.0 | 14.7 | 8.7 | 12.3 | 11.7 | 12.6 | - | | 10.5 | 12.0 | - | N |
| No. 4 | 8.3 | 12.9 | 23.4 | 22.8 | 14.8 | 15.4 | 28.7 | 17.6 | - | | 24.4 | 10.1 | - | HI |
| No. 5 | 4.4 | 8.7 | 23.6 | 31.5 | 22.1 | 19.9 | 23.8 | 30.1 | - | | 20.3 | 10.2 | - | HI |
| No. 6 | 10.9 | 11.7 | 12.4 | 15.4 | 13.3 | 17.4 | 19.7 | 22.1 | - | | 25.4 | 14.4 | - | HI |
| No. 7 | - | - | 4.3 | 8.7 | 25.2 | 12.8 | 19.4 | 30.9 | - | | 18.2 | - | - | HI |
| No. 8 | 5.8 | 4.5 | 6.1 | 9.3 | 17.0 | 31.4 | 17.3 | 19.4 | 23.6 | | 17.1 | 8.1 | 13.4 | HI |
| No. 9 | 13.2 | 5.6 | 9.7 | 16.0 | 14.8 | 20.7 | 22.5 | 18.7 | 11.8 | | 22.9 | 11.6 | 6.8 | HI |
| No. 10 | - | - | 15.1 | 16.6 | 35.4 | 20.4 | 32.2 | 29.2 | - | | 11.6 | 8.0 | 6.9 | HII |
| No. 11 | - | 4.2 | 17.1 | 12.8 | 14.1 | 12.0 | 16.1 | 15.2 | 8.5 | | 5.6 | 6.6 | 5.6 | HII |
| No. 12 | - | - | 5.4 | 11.7 | 11.5 | 15.2 | 19.7 | - | - | | - | - | - | HII |
| No. 13 | - | 13.1 | 19.1 | 11.7 | - | 13.2 | 8.3 | 14.6 | - | | 12.2 | 6.1 | - | HII |
| No. 14 | 6.2 | - | 4.5 | 14.7 | 9.5 | 9.1 | 8.3 | 19.3 | 18.3 | | 18.9 | 9.9 | - | HII |
| No. 15 | 3.8 | 5.0 | 11.2 | 19.6 | 23.0 | 11.6 | 11.0 | 17.8 | 13.8 | | 16.4 | 9.1 | 12.7 | HII |
| No. 16 | - | - | 4.4 | 10.2 | 16.7 | 24.3 | 22.3 | 17.0 | - | | 16.7 | 12.2 | - | HII |
| No. 17 | - | - | - | 15.1 | - | 21.6 | 12.9 | 23.7 | - | | 18.2 | 16.8 | - | HII |
| No. 18 | - | 9.6 | 7.8 | 11.2 | 30.3 | 11.7 | 15.1 | 17.5 | - | | 13.7 | - | - | HII |
| Mean | 7.9 | 7.9 | 11.7 | 14.8 | 18.2 | 17.2 | 17.7 | 20.3 | 15.9 | 18.7 | 16.0 | 10.2 | 8.6 | |
| S.D. | 2.87 | 3.24 | 6.50 | 5.91 | 7.36 | 5.66 | 6.62 | 5.64 | 5.56 | | 5.60 | 3.17 | 3.51 | |
| S.E. | 0.91 | 0.94 | 1.58 | 1.40 | 1.84 | 1.33 | 1.56 | 1.37 | 2.27 | | 1.36 | 0.82 | 1.43 | |

N = Normotensive Group
HI= Hypertension I Group
HII= Hypertension II Group

## SUMMARY OF ANTE-NATAL PROGRESS AND DELIVERY OF THE PATIENTS

(Excluding the special cases described separately in the text)

1. Occupation

Housewives made up 38.5% of the normotensive group, 20.8% of the hypertension I group and 33.3% of the hypertension II group. Of the remainder, the majority worked as clerks or secretaries and made up 38.5%, 50% and 38.9% of the respective groups.

2. Anaemia

This has been dealt with in the section giving the haemoglobin results.

3. Urinary infection and Albuminuria

One patient in the normotensive group, four in the hypertension I group and five in the hypertension II group developed urinary infections in pregnancy. Albuminuria in the absence of infection occurred in three of the hypertension I group and five of the hypertension II group.

4. Investigation of glucose tolerance

All patients who exhibited one of the criteria for investigation of glucose tolerance, as described by Wright, Dixon and Joplin (1968), had glucose and prednisone tolerance tests carried out. The results were interpreted personally by these workers according to the recommendations of the British Diabetic Association. Of the two subjects tested from the normotensive group one patient had a normal test result and the other had renal glycosuria. Of the

seven subjects from the hypertension II group two patients had normal test results, four had renal glycosuria and one had latent diabetes. The latter patient developed hypertension and albuminuria for which labour was induced before term and therefore she was included in the hypertension II group. Foetal distress necessitated delivery of this patient by Caesarean Section. One other patient diagnosed as having latent diabetes remained normotensive throughout but her case is described separately.

ANTE-NATAL ADMISSION TO HOSPITAL

1. Hypertension

In the hypertension I group 66.7% of the patients required admission in the second half of pregnancy in addition to earlier admissions for investigation; 45.8% required induction of labour.

In the hypertension II group 33.3% of the patients were admitted for treatment in late pregnancy and all had labour induced. None of the patients had fore-arm and handflow rates estimated after therapy had commenced.

2. Ante-Partum Haemorrhage

A slight ante-partum haemorrhage of unknown origin was the reason for admission of one normotensive patient and one who developed hypertension later. In one patient a small haemorrhage occurred while she was an in-patient with hypertension late in pregnancy. And her patient in the hypertension II group had a cervical carcinoma-in-situ and bled slightly from the cervix.

3. Other

Four patients in the normotensive group, three in the hypertension I group and seven in the hypertension II group were admitted

to hospital because of hyperemesis, threatened abortion, urinary infection or rhesus iso-immunisation.

DELIVERY

88.5% of the normotensive group, 70.8% of the hypertension I group and 63.9% of the hypertension II group were delivered normally. (A significant difference exists between the normotensive and the hypertension II group; $\chi^2 = 4.74$ on 1 degree of freedom, $0.05 > P > 0.02$.) Three of the normotensive group, five of the hypertension I group and ten of the hypertension II group were delivered by forceps. Two of the hypertension I group had breech deliveries and one of the hypertension II group was delivered by Caesarean Section.

Two of the hypertension I group and one of the hypertension II group required treatment with Avertin in labour and puerperium because of uncontrolled hypertension. One patient in the hypertension I group had a fit of the grand mal type six weeks after delivery. An E.E.G. showed changes compatible with epilepsy.

Subsequent Deliveries

Seven of the normotensive group were subsequently delivered in this hospital. Four remained normotensive and three would have been included in the hypertension I group. Seven of the hypertension I group were delivered again. Two of these were normotensive and the other five retained their classification. Eight of the hypertension II group were delivered again, only two of these were normotensive and the rest would have been included in the hypertension I group.

## SPECIFICATIONS AND ADDRESSES OF SUPPLIERS OF APPARATUS.

1. Recorder.

   Bristol Dynamaster twin channel potentiometric recorder. P.132256. 4 r.p.m. motor. 240 volts. 50 cycles mains.

   Elliott Bros. Ltd., Century Works, Lewisham, London, S.E.13.

2. Circulating Pump.

   Type C15/50.

   Charles Austen Pumps Ltd., 100 Royston Road, Byfleet, Surrey.

3. Stirrer Pump.

   W.M.140. Water immersion pump.

   Gallenkamp, Technico House, Christopher Street, London, E.C.2.

4. Heater.

   Type C 305E. Tinned brass. 100 watts. 24 volts.

   Hedin Ltd., Heating Element Division, Raven Road, South Woodford, London, E.18.

5. Thermostat.

   Standard cartridge 318 - to work to 37°C.

   Ether Ltd., Electromethods, Caxton Lane, Stevenage, Herts.

6. Thermistor Probes.

   Yellow Springs Instrument Co. Inc., Yellow Springs, Ohio, U.S.A.

7. Plethysmograph sleeves and plastic sand-bags.

   Plysu Industrial Ltd., Woburn Sands, Bletchley, Buckinghamshire.

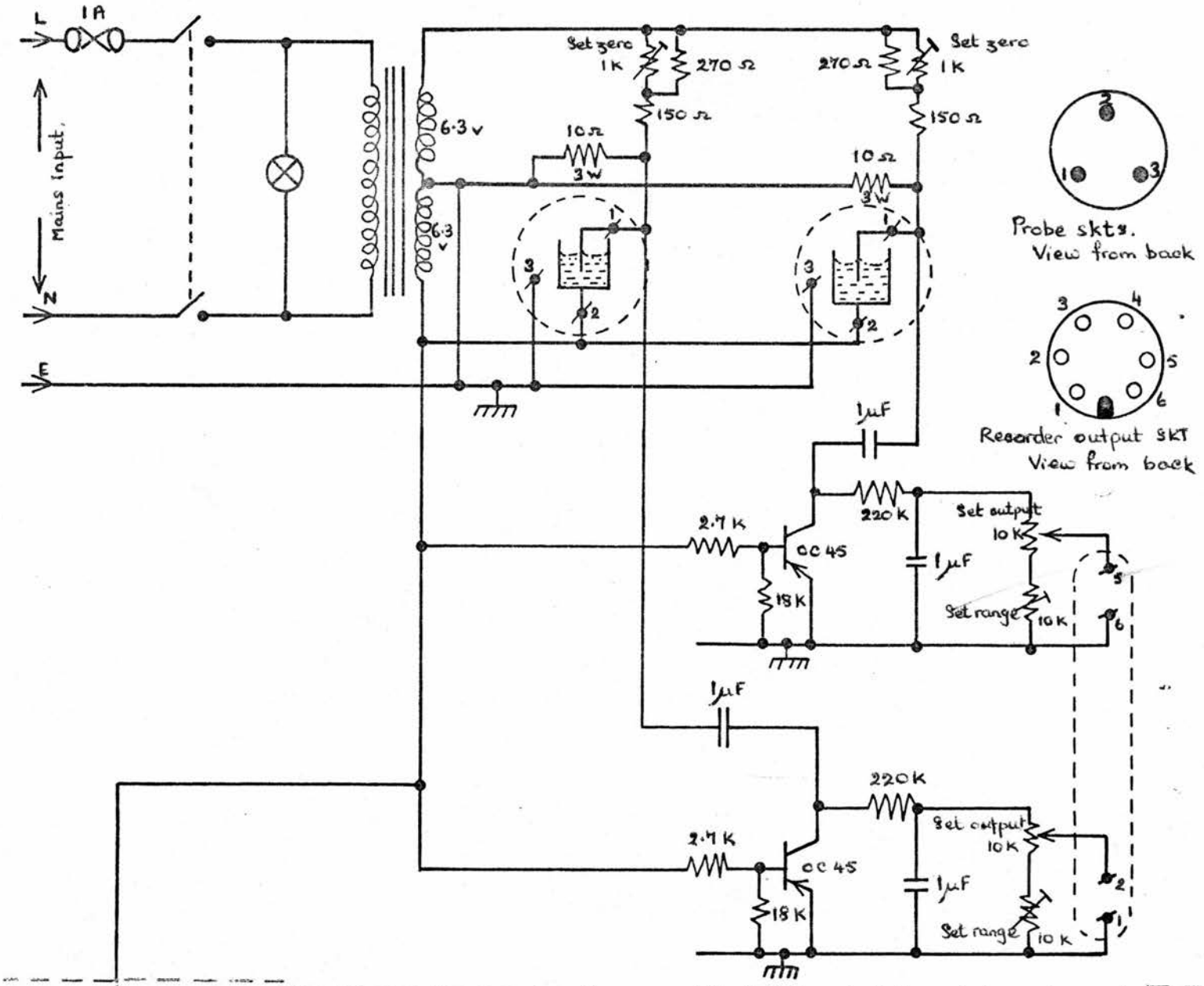
8. Air-conditioning.

   Rootes Tempair from Raymond Ball (Shirley) Ltd., 826 Wickham Road, Shirley, Croydon, Surrey.

9. Micro-haematocrit apparatus.

   Hawksley and Son, Ltd., London.

## Limb Plethysmograph Circuit

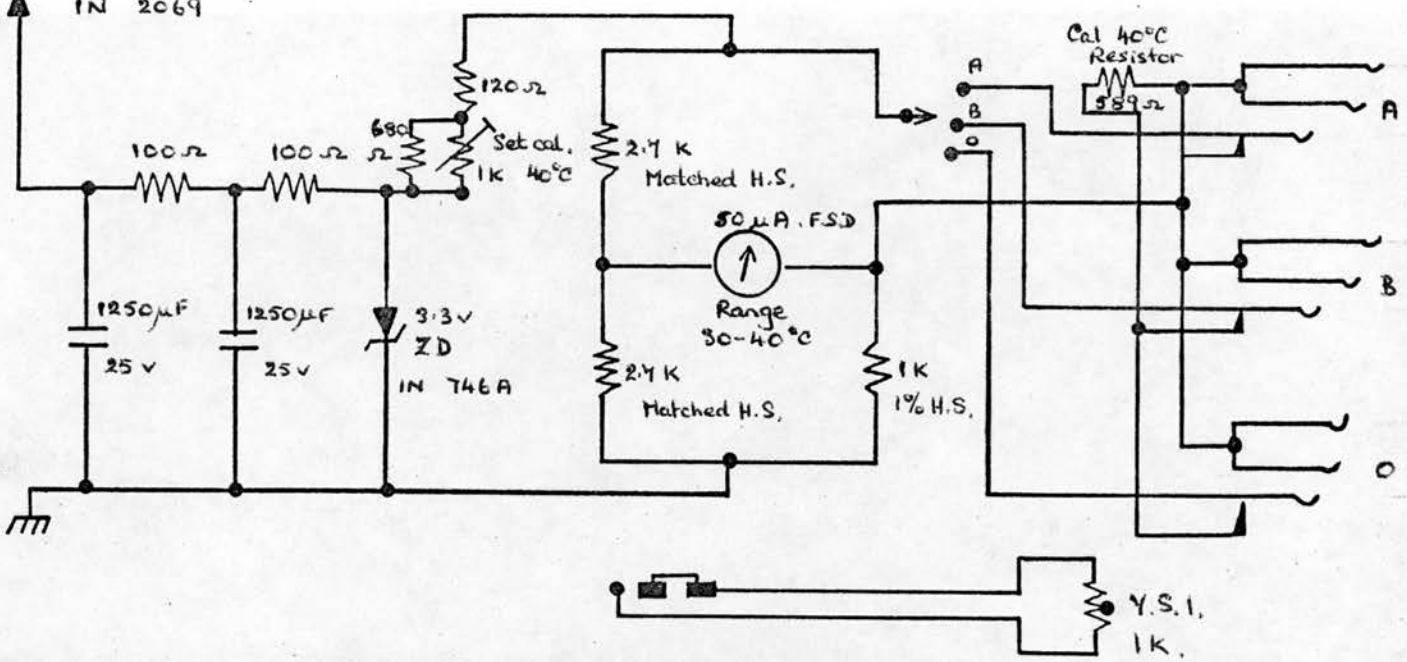



Probe skts.
View from back




Recorder output SKT
View from back

Thermistor thermometer for use with Y.S.I. 1 K thermistors in probes.



## ACKNOWLEDGEMENTS

I am deeply indebted to the Medical Research Council for providing a personal grant for this research and to Professor J. C. McClure Browne, in whose Department the work was carried out, for providing facilities and encouragement.

My supervisor, Mr. W. G. MacGregor, was largely responsible for initiating me into thie field of research and for his continued interest and guidance, I am profoundly grateful.

Also, I should like to record my thanks to Dr. H. Payling Wright for her invaluable assistance in the early stages of this study and for introducing me to research techniques.

Dr. O. G. Edholm and Dr. R. Fox of the Division of Human Physiology, Medical Research Council, gave valuable technical advice at the onset of the study and I am very grateful for their continued interest.

Mr. M. Hills of the Department of Medical Statistics and Epidemiology of the University of London most kindly gave advice and assistance in the statistical analysis. Miss Christine Bramley, formerly of the Medical Research Council Computer Services Centre, was responsible for preparing most helpful computerised tables for assistance with calculations of the flow curves.

My thanks are also due to Mr. C. Loudon and Mr. J. Fox and their excellent staff, for assembling and maintaining the apparatus, and to Mr. E. Simmons and Mrs. Carol Stafford of the Obstetric Laboratories, Hammersmith Hospital, for assistance with the haematology and Evans Blue extractions.

I am very grateful to Dr. Erica Wachtel for her assessment of the vaginal cytology and to Dr. K. Fotherby for supervising the pregnanediol extractions.

I greatly appreciate the co-operation given by Miss C. Miller and the Midwifery Staff of Hammersmith Hospital and above all the assistance and interest given by Miss Agnes Mulligan and Mrs. Barbara Jones who were entirely responsible for the nursing care of the patients involved in this research.

It is a pleasure to record my deep appreciation to the many willing and co-operative patients and staff who took part in these investigations.

Finally, I should like to thank Miss Janet Baines for her excellent work in typing the manuscript.